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Changing Concepts in the Therapy of Lung Abscess: A Twenty Year Survey

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Worsening in the prognosis of patients with lung abscess in the past four years prompted us to bring our previous observations[1] to date. The 15 years from 1941 to 1955 in our experience, were marked by steady and dramatic improvement in the results in this disease. In the past four years this trend has been reversed.

Material and Method of Treatment

This series consists of 87 cases; these can be divided readily into four groups (Table 1). Group A: 1941-1944; 19 cases; Group B: 1945-1951: 29; Group C: 1952-1955: 17; Group D: 1955 to date: 22.

Group A: 1941-1944: The Sulfonamide Period; treatment consisted of supportive measures, bronchoscopic aspirations, postural drainage, sulfonamides and surgical procedures. Bronchoscopy was used routinely in all cases, both as a diagnostic tool and also as a means of cleansing the tracheal bronchial tree. Sulfathiazole and sulfadiazine were used in various dosages. Surgical procedures were simple incision and drainage or two stage pneumonotomies.

Group B: 1945-1951: The Penicillin Period; this drug was used both parenterally and by aerosol. Supportive treatment was unchanged. Surgical procedures were the same as Group A except from 1949 on, resection was carried out in the majority of cases requiring surgical intervention.

Group C: 1952-1955: The Antibiotic and Trypsin‡ Period; supportive treatment remained unchanged. The antibiotics used were oxytetracycline, and penicillin. The drug used was selected from sensitivity studies of material obtained at bronchoscopy. Aerosol trypsin administration in a dosage of 125 mg. in 2 cc. of diluent daily, was used in each instance for five to ten days and then every second day for a period of from two to four weeks. Surgery during this period was resectional. No surgical drainage procedure was done.

Group D: 1955-1959: The Iatrogenic Period; supportive treatment remained unchanged. Culture and sensitivity studies determined the anti-

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‡Tryptar—Armour Company brand of trypsin.

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TABLE 1—LUNG ABSCESS GROUPS

	A	B	C	D	Total
Groups	1941-44	1945-51	1952-55	1956-59	1941-59
Cases	19	29	17	22	87

TABLE 2—ETIOLOGIC FACTORS

Groups	A	B	C	D
1. Unconsciousness				
a. Anesthesia	3	1	2	1
b. Alcohol			2	9
c. Convulsion			1	
d. Cerebral Vascular Accident				1
2. Pulmonary Infection				
a. Pneumonia	4	8	2	6
b. Upper Respiratory Infections	5	4	3	
c. Influenza		1	2	1
3. Foreign Body		1		
4. Injuries		2		
5. Idiopathic	7	12	5	5

biotic of choice. Aerosol trypsin was used in essentially the same routine as Group C. Surgery, when indicated, was either resectional or drainage.

Pathogenesis and Etiology

Our concept of pathogenesis and etiology remains unchanged from our previous report.[1] It is our belief that bronchial, or bronchiolar obstruction by any one of several causes, i.e., foreign body, inflammation or aspirated secretions, leads to an area of atelectasis which when followed by infection leads to vessel thrombosis and this then to an area of infarction. Infection plus infarction leads to tissue necrosis and suppuration.[2,3,4,5] Table 2 shows the distribution of the believed etiologic factors in each of the four groups, this shows no significant difference in these groups.

Bacteriology

The majority of cases had nonpathogenic organisms on culture; this is in line with our previous experience along with that of others.[1,3] How-

TABLE 3—BACTERIOLOGY

Groups	A	B	C	D
Alpha streptococci	3	8	12	15
Staph. albus	5	3	1	
Diplococcus pneumoniae	3	3	1	
Beta streptococci	1	3	2	
Staph. aureus	2	3	1	7
Enterococci	1	2	1	1
M. catarrhalis		1	1	3
Candida albicans		1	2	
Klebsiella pneumoniae		1	2	3
H. influenzae				
Serratia			1	
Herrellea			1	
Pseudomonus				6
Micro aerophilic Streptococci				2

TABLE 4—MORTALITY

Groups	A	B	C	D
Died	6 of 19	5 of 29	0 of 17	8 of 22
Percent	31.5	17.2	0	36.3

ever, in Group D the incidence of *Staphylococcus aureus*, and *Pseudomonas aeruginosa* was much higher than in any of the other groups. This, we believe, is of extreme importance in the changing prognosis noted in the last four years.

Results

Mortality figures are shown in Table 4. The figure of 31.5 per cent in the 1941 to 1944 period (Group A) was generally in line with the mortality figures at that time. With the advent of penicillin in 1945 to 1952 (Group B) there was for the first time a significant drop in mortality to 17.2 per cent. Group C, 1952 to 1955 with no mortality was encouraging.

Group D, 1955 to the present, was a considerable surprise and disappointment to us, with a mortality of 36.3 per cent, putting us back to the pre-antibiotic period.

Discussion

Several factors contributed to the improvement in the treatment of lung abscesses in the first 15 years of this period. Perhaps of greatest importance was the availability of effective antibiotics and the use of aerosol trypsin as a means of promoting continual and adequate drainage of these abscesses. The development of segmental resection and lobectomy to the point of perfection in the past decade, undoubtedly, played a role in the satisfying improvement in mortality. The regression to pre-antibiotic days with a mortality of 36.3 per cent in the group D period, we believe, could well be attributed to the following iatrogenic causes. Two of the three patients receiving corticoids for various reasons died with lung abscess. The rise in the incidence of *Staphylococcus aureus hemolyticus*, as an etiologic agent, is of great importance as four of the six patients with this organism died. The *Staphylococcus aureus* problem may well be the result of the indiscriminate use of broad spectrum antibiotics.

Our indication for resection in lung abscess is a residual thick walled cavity which fails to show continued clearing over a three week period. We have been content to follow carefully patients with thin walled cavities and have now observed six such patients for periods up to one and one half years and have noted closures in all between four months and one and a half years.

There were only two surgical cases among the 22 in Group D. The trend toward less frequent surgery was first noted in Group C when six of 17 patients required surgical intervention. We believe this is because of more potent antibiotics, the early use of bronchoscopy, and the use of trypsin to promote and continue adequate drainage. Furthermore, our observation that thin walled cavities may be safely followed has reduced our surgical cases.

SUMMARY

1. The prognosis of lung abscess has worsened in the past four years. This is believed to be primarily due to such iatrogenic causes as hospital staphylococcus and increased use of corticoids.

2. Aerosol trypsin remains in our hands at least a helpful therapeutic agent.

3. Thin-walled residual cavities may be safely followed with good expectation that they will heal.

RESUMEN

1. El Pronóstico del absceso pulmonar, ha empeorado en los últimos cuatro años. Se cree que esto se debe a causas iatrogénicas tales como el estafilococo de los hospitales y el aumento del uso de los corticoides.

2. El aerosol de tripsina permanece en nuestras manos cuando menos como agente terapéutico útil.

3. Las cavidades de paredes delgadas pueden observarse con seguridad con la posibilidad en que curen.

RESUMÉ

1. Le pronostic des abcès du poumon s'est assombri dans ces quatre dernières années. On croit que ceci est dû d'abord à des causes en rapport avec l'action des médecins, telles que la fréquence du staphylocoque dans le milieu hospitalier, et l'ultilisation accrue des corticoïdes.

2. La trypsine en aérosols reste au moins entre nos mains un agent thérapeutique plein de promesses.

3. Des cavités résiduelles à parois minces peuvent être suivies avec de bonnes chances de guérison.

ZUSAMMENFASSUNG

1. Die Prognose des Lungenabszesses hat sich in den letzten 4 Jahren verschlechtert. Es besteht die Ansicht, daß dies in erster Linie die Folge von so iatrogenen Ursachen ist, wie Krankenhausinfektion mit Staphylokokken und erhöhtem Gebrauch von Korticoiden.

2. Aerosol-Trypsin bleibt in unserer Hand wenigstens eine nützliche therapeutische Substanz.

3. Dünnwandige Restcavernen kann man vorsichtig überwachen in der gültigen Erwartung, daß sie heilen werden.

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SYSTEMIC BLOOD PRESSURE IN CHRONIC BRONCHOPULMONARY INSUFFICIENCY

The authors studied 120 subjects with chronic lung disease. They found that the systemic blood pressure was constantly and significantly lower than the normal range (about 15 per cent). They suggest that the lowering of blood pressure is due to a marked increase in the bronchial arterial flow, resulting in a shunt between the systemic and pulmonary circulation.

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INHALANT RESPIRATORY ALLERGY WITH NEGATIVE CUTANEOUS REACTIONS

Refractoriness to pollen and nonpollen inhalant allergens by skin test in patients with respiratory allergies is a definite clinical entity, the author states. The diagnosis is primarily based on the clinical history of recurrent symptoms of intolerance to pollens and other inhalant allergens. Of significant clinical interest is the observation that these patients with skin test inhalant negative reactions, especially to pollens, are invariably asthmatics. The treatment of such patients is of clinical and extreme practical importance because they require considerably higher top doses of specific allergenic extracts for relief of symptoms than the patients with skin test positive reactions to corresponding inhalant allergens. The results of treatment with allergenic inhalant extracts in the skin test negative reactors are as good if not better than the results obtained with corresponding allergenic extracts in the skin test positive reactors. The optimal protective doses of allergenic extracts for the skin negative reactors are the same both for children and adults. In the light of our experience, the effectiveness of pollen or other inhalant allergenic therapy for persons with respiratory allergy with negative cutaneous reactions to these allergens is based solely on specific immunization.

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Pulmonary Resection in the Treatment of Tuberculosis*,**

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Pulmonary resection has evolved as the treatment of choice in certain clinicopathologic entities of pulmonary tuberculosis. However, the precise roles of resective and non-resective therapy will ultimately be determined through analysis of the results obtained by these forms of treatment. Therefore, it seems important to report current experiences in the treatment of pulmonary tuberculosis. The present study is a critical analysis of 268 consecutive pulmonary resections for proved pulmonary tuberculosis.

Clinical Material

In the interval between the opening of the Middle Tennessee Tuberculosis Hospital in September, 1954 and January 1, 1958, there were 1667 hospital admissions. During this period, 296 pulmonary resections were performed; in 268 instances the resection was for proved pulmonary tuberculosis. The diagnosis was established either by preoperative identification of the tubercle bacillus in the sputum (smear or culture) or gastric aspirate (culture) or by postoperative histologic or bacteriologic study of the resected specimen.

Preoperative Data

The 268 pulmonary resections for tuberculosis were performed in 252 patients. An analysis of these patients revealed: 90 white females, 43 Negro females, 91 white males and 44 Negro males. The ages ranged from five to 66 years with 79 per cent falling in the 20 to 49 year groups. Eighty per cent of the females were under 40 years of age at the time of resection whereas 58 per cent of the males were over 40 years of age at the time of resection.

Almost half of the patients (49 per cent) had pulmonary tuberculosis for more than two years before the resection, and in 35 per cent the disease dated back more than four years. In 28 per cent the disease had been present less than one year. The limitations of these figures should be pointed out as they are based on the time between the patients' recollection of the first symptoms and the pulmonary resection. Many coming to pulmonary resection represented failures of prolonged antituberculosis drugs as well as non-resective surgical treatment: 12 had undergone previous thoracoplasty, 10 had received pneumothorax and phrenicectomy, 21 had undergone phrenicectomy alone, 10 had received pneumothorax alone and 35 had been treated by pneumoperitoneum.

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TABLE 1—BACTERIOLOGIC RELATIONSHIP OF SPUTUM TO RESECTED SPECIMEN

Status of Sputum Immediately Preoperative*	Specimen Smear+		Specimen Culture+	
	No.	per cent	No.	per cent
+ 76	73	96	51	67
− 189	139	74	33	17
	212	79	84	31

*Concentrate Smears

Stabilization of the pneumonitic process by antituberculosis agents, bed rest and general supportive measures administered over at least a six month period was practiced except in instances where there was a possibility of malignancy masquerading as pulmonary tuberculosis. An analysis of the preoperative drug therapy was complicated by the fact that many patients had been treated in another hospital or at home and did not receive the full six months regimen in this hospital. There were 116 receiving six months of continuous preoperative drug therapy in the Middle Tennessee Tuberculosis Hospital who had the following treatment: most patients received INH (over 90 per cent) and/or PAS (over 80 per cent); therapy was limited to two drugs in 63 per cent. Of these patients, 110 had positive sputum on admission and although 72 per cent became sputum negative, 85 per cent had an open cavity at the time of surgery and 81 per cent had a positive smear on examination of the resected specimen. The results in the pneumoperitoneum group revealed that 25 of the 35 became sputum negative (71 per cent) and 86 per cent had an open cavity at the time of resection. It should be pointed out that these figures do not take into consideration the extent of the disease prior to institution of therapy.

Analysis of the bacteriologic findings revealed that 76 patients (28 per cent) were sputum positive at the time of resection (Table 1). However, this correlates poorly with finding of a positive smear in 212 (79 per cent) of the resected specimens. A better correlation is found in the 84 (31 per

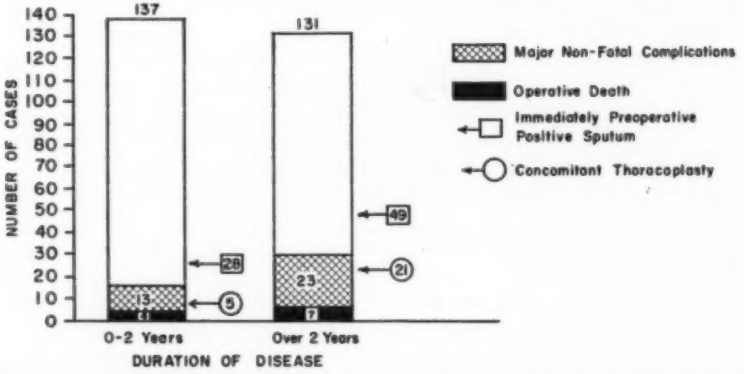

FIGURE 1: Complications and deaths are tabulated according to duration of the disease process and found to be twice as frequent in the patients with a longer history of tuberculosis. The high incidence of positive preoperative sputum is noted in patients with tuberculosis for more than two years.

TABLE 2—RESECTION IN THE TREATMENT OF PULMONARY TUBERCULOSIS—EXPERIENCE BY YEAR

Extent of Resection	1954	1955	1956	1957	Total
Wedge	1	1	7	3	12
Segment(s)	3	13	15	25	56
Lobectomy	6	35	44	47	132
Lobectomy+	0	13	15	4	32
Bilobectomy	0	3	6	6	12
Pneumonectomy	1	5	10	8	24
Total	11	70	97	90	268
Major Complications (Patients)	4	7	18	18	47 (18 per cent)
Operative Deaths	0	2	3	6	11 (4 per cent)

cent) positive cultures from the resected specimens: a comparison of the preoperative sputum status and results of bacteriologic study of the resected specimen is of interest. Of the 76 instances of positive preoperative sputum, the resected specimen yielded positive smear in 73 and positive culture in only 51 instances. Of the 189 instances of negative preoperative sputum, the specimen gave positive smear in 139 and positive culture in 33.

Pulmonary function studies were routinely performed preoperatively. Twenty-nine per cent of the patients had a maximum breathing capacity (MBC) of less than 60 per cent of normal and 22 per cent had a vital capacity (VC) of less than 60 per cent of normal. Values of less than 50 per cent of normal were found in 13 per cent for the MBC and 6 per cent for the vital capacity.

In addition to frequent roentgenograms of the chest, planigrams to demonstrate questionable cavities and bronchograms for the demonstration of stenotic or bronchiectatic changes were performed in many patients. Preoperative bronchoscopy was carried out routinely; bronchospirometry was performed in selected cases.

TABLE 3—MAJOR POSTOPERATIVE COMPLICATIONS IN 252 PATIENTS UNDERGOING 268 PULMONARY RESECTIONS FOR TUBERCULOSIS

	Number	Number Fatal	Days Postoperative at Death
Bronchopleural Fistula	18		
Hemothorax	7		
Tuberculous Spread	6	2	21,60
Pleural Space Problem (not BPF*)	5		
Empyema (without BPF*)	5		
Respiratory Insufficiency	3	3	4,10,23
Cardiac Arrhythmia	3		
Homologous Serum Jaundice	2		
Pulmonary Embolus	2	2	4,20
Cardiac Arrest	2	2	1,27
Cardiovascular Collapse	1	1	1
Tracheal Stenosis	1	1	78
	55 (47 Patients)	11	

*Bronchopleural Fistula

TABLE 4—RELATION OF SELECTED COMPLICATIONS TO DURATION OF DISEASE

Complications	Duration of Disease 0-2 years	over 2 years
Bronchopleural Fistula	6	12
Tuberculous Spread	2	4
Empyema (without BPF*)	1	4
Pleural Space Problem (without BPF*)	4	1
Hemothorax	2	5

*Bronchopleural Fistula

In general the following features served as the prime indications for resective treatment: (1) persistent cavity; (2) persistent infiltrate with positive sputum; (3) tuberculoma; (4) bronchostenosis or, (5) destroyed lung. Persistent cavity was by far the most common single indication for surgery; cavity was present in over 80 per cent of the resected specimens.

Operative Data

The number and extent of resections performed each year of the study is recorded in Table 2. The figures given for 1954 represent only a part of the year because the hospital did not open until the month of September. The total of 268 pulmonary resections were performed in 252 patients. Sixteen had two resections; in 12 instances the second resection was contralateral and was performed within 10 months after the first. Lobectomy has been the most commonly performed pulmonary resection during each year of this study. The yearly incidence of wedge or segmental resection appears to be increasing while resections of more than a single lobe seem to be decreasing. Thoracoplasty was performed at the time of pulmonary resection in 28 instances while in six patients, preliminary thoracoplasty had been done. Thus 13 per cent of the patients had thoracoplasty in conjunction with their pulmonary resection. In 31 (91 per cent) of the 34 patients undergoing thoracoplasty, the pulmonary resection involved

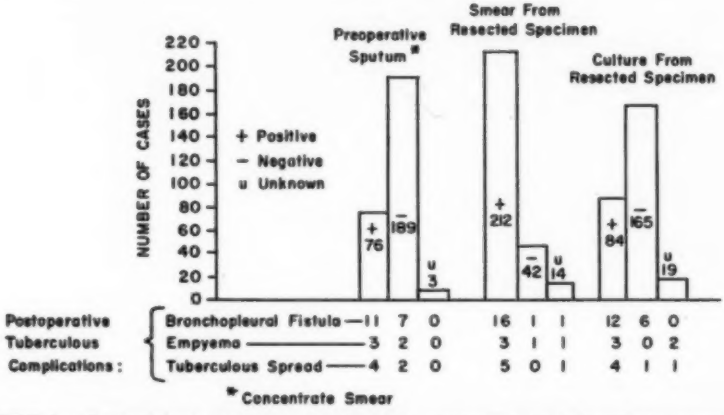

FIGURE 2: Bacteriologic studies are related to postoperative tuberculous complications. Such complications were four times as common in patients with a positive preoperative sputum as in the sputum negative group.

TABLE 5—PZA THERAPY AS RELATED TO POSTOPERATIVE TUBERCULOUS COMPLICATIONS

	PZA Group	Non-PZA Group
Patients	51	212
Tuberculous Spread	0	6
Empyema	0	5
Bronchopleural Fistula	6	12

an upper lobe. However, in the entire series of 252 patients the resection involved an upper lobe in 226 (90 per cent).

Lobectomy was more commonly performed in those in whom the disease process had been present less than two years, while pneumonectomy was more common in patients with pulmonary tuberculosis for more than two years. The other types of resection were just as common in those with the disease less than two years as in patients with a longer history of pulmonary tuberculosis. Thoracoplasty in conjunction with pulmonary resection was more common in those with pulmonary tuberculosis for more than two years; 28 of the 34 thoracoplasties were performed in this group.

In addition to the 268 pulmonary resections analyzed in this report there were three patients in whom a pneumonectomy was attempted but not done. Because of undue hazard or sudden vasomotor collapse, the procedure was terminated prior to completion of the resection. Bronchopleural fistula developed in two of these three patients; however, all three survived.

Complications

The major complications and operative deaths in each year of the study are recorded in Table 2. The numbers given for major complications represent patients rather than total number of complications; some had more than one major complication. The term, operative death, is used to mean all deaths attributable to the operative procedure even though death may have occurred months after the operation. The incidence of major complications in 1956 and 1957 was significantly greater than in 1955; the death rate in 1957 increased over that of 1955 and 1956. The incidence of the extent of resection shows no significant variation from year to year.

Table 3 lists the total number of major complications, indicates which complications were fatal and in the fatal ones records the postoperative day on which the fatality occurred. A word of explanation is necessary in

TABLE 6—PREOPERATIVE VITAL CAPACITY AND MAXIMUM BREATHING CAPACITY VERSUS OPERATIVE COMPLICATIONS AND DEATHS

	Range of Values	Patients	Complications No.	Complications per cent	Deaths No.	Deaths per cent
Vital Capacity	<60 per cent of Normal	41	13	32	7*	17
	⩾60 per cent of Normal	150	18	12	1	0.7
Maximum Breathing Capacity	<60 per cent of Normal	54	16	30	5*	9
	⩾60 per cent of Normal	137	15	11	3	2

*Two deaths attributed to respiratory insufficiency.

TABLE 7—ANALYSIS OF POSTOPERATIVE BRONCHOPLEURAL FISTULA AND RESULTS OF TREATMENT

Treatment	Extent of Resection			Result of Treatment	
	Segment(s)	Lobectomy	Lobectomy+	Healed	Persistent
Tube Alone	3	3	1	2	5
Thoracoplasty	2	4	2	6	2
Thoracoplasty and Suture Fistula	2	0	0	1	1
Suture Fistula	1	0	0	1	0
	8	7	3	10	8*

Lobectomy+ = less than bilobectomy

*Three patients died in follow-up period with persistent fistula.

regard to certain complications. Empyema indicates a tuberculous pleural space infection in the absence of bronchopleural fistula. Similarly those complications listed as space problems did not involve a demonstrable bronchopleural fistula. A complication resulting in a fatality was often one of several encountered by a patient and an arbitrary designation of the critical complication was sometimes required. Bronchopleural fistula was the most common complication comprising 18 (33 per cent) of the total of 55 complications and had an incidence of 7 per cent in the total of 268 resections. Tuberculous spread occurred in 6 (2 per cent) of the patients and empyema as well as pleural space problems and hemothorax each had a similar incidence. The case of tracheal stenosis followed a right pneumonectomy and subsequent operative procedures to correct

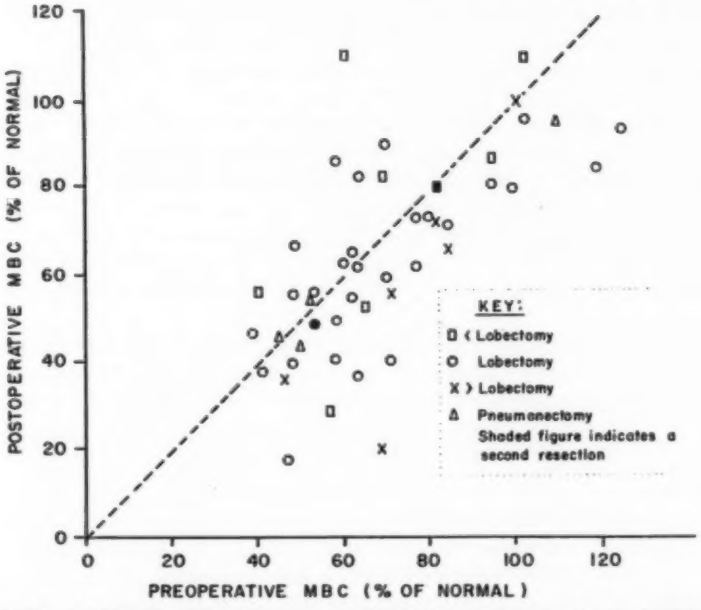

FIGURE 3: Maximum breathing capacity (MBC) in the preoperative and postoperative period is contrasted. Figures appearing below the broken line indicate a decrease in function and above an increase. The vertical distance from the broken line represents the amount of increase or decrease.

TABLE 8—RESULTS OF TREATMENT OF THE COMMON MAJOR COMPLICATION

	Number	Results of Treatment		
		Complete Recovery	Unchanged	Died
BPF	18	10	5	3
Tuberculous Spread	6	4	—	2
Empyema (without BPF*)	5	3	1	1
Hemothorax	7	7	—	—
Pleural Space Problem (without BPF*)	5	5	—	—

*Bronchopleural fistula

the stenosis failed. This patient was not counted among the bronchopleural fistula even though a fistula existed following the failure of a dermal patch graft.

A tabulation of the relationship of age to major complications and deaths revealed that the incidences of major complication under 30 years of age was 9 per cent, whereas major complications occurred in 22 per cent of the patients 30 years of age or older. However, these figures are probably influenced by the fact that more extensive pulmonary resections were generally performed in the older age group. Only 19 per cent of the younger group underwent resections greater than lobectomy while 31 per cent of the resections in the older age group were greater than lobectomy.

Complications and deaths were more common in the 135 males than the 133 females (34/13 for the complications and 7/4 for the deaths). The complication rate was about the same for Negroes and whites, but the death rate was far higher in the Negro—8 per cent as compared to 2 per cent. The total of 11 deaths is relatively small and four deaths in Negroes following pneumonectomy raise the Negro death rate. Pneumonectomy was more than twice as common in the Negro group and of the five deaths following pneumonectomy four of them were in Negro patients. In comparing the other types of resection by race, the following facts emerge: the incidence of lobectomy was equal in Negro and white, resections less than lobectomy were more common in the white patients and resections of more than lobectomy were more common in the Negro. In the breakdown of patients by age, it has already been noted that the female was generally younger than the males; this was true for both the Negro and white groups.

In contrasting the duration of the disease process with the incidence of complications and deaths. Figure 1 presents the following data: there were roughly equal numbers of patients with a history of less than and more than two years' duration, complications and deaths were almost twice as frequent in the group with the longer history, a positive sputum

TABLE 9—POSTOPERATIVE BACTERIOLOGIC* FOLLOW-UP DURING HOSPITALIZATION

Number of Patients	Negative	Positive 1 or 2+	Positive >2+	Unknown
242	190	30	18	4

*Sputum concentrate smears

TABLE 10—ANTITUBERCULOSIS MEDICATION IN THE FOLLOW-UP PERIOD

	1 Year		2 Years		3 Years		4 Years		5 Years	
	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent
On Drugs	172	87	48	30	20	18	6	12	0	0
Off Drugs	26		112		90		41		8	

immediately preoperatively was also almost twice as common in the group with the longer history, and finally a concomitant thoracoplasty was more common in these patients with pulmonary tuberculosis of more than two years' duration. Further breakdown of extent of resection as related to duration of disease was made and it is of interest that there was no difference in the patients with less than a one year history and those with a one to two year history except that pneumonectomy was more common in the patients with a history of one to two years. There was no significant difference of the extent of resection in the patients with history of tuberculosis for two to four years, four to eight years and more than eight years.

Certain complications were related to duration of the disease process (Table 4). It was of interest that only pleural space problems predominated in the group with the shorter duration of disease. Bronchopleural fistula, tuberculous spread, empyema and hemothorax were much more common in those patients with pulmonary tuberculosis for more than two years. In the other complications, there was not a significant difference between the two groups.

Inasmuch as the vast majority of the patients received essentially the same drug therapy in the preoperative period, it was not possible to relate complications to preoperative drug therapy in a meaningful way.

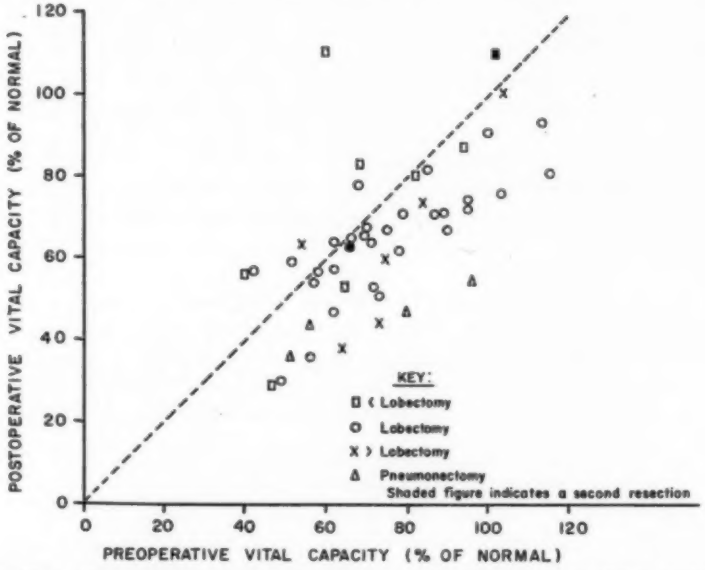

FIGURE 4: Vital capacity in the preoperative and postoperative period is contrasted. Most patients sustained a decrease in vital capacity.

However, the effectiveness of PZA (pyrazinamide) in the prevention of postoperative complications could be ascertained. In a group of 51 patients, PZA therapy was initiated two weeks prior to resection and continued two to three months postoperatively. In none of these 51 patients was there evidence of tuberculous spread or empyema. In contrast, tuberculous spread occurred in six patients and tuberculous empyema in five of 212 patients not receiving PZA. However, the incidence of bronchopleural fistula was greater in the PZA group (Table 5).

The relationship of the bacteriologic status of the preoperative sputum and the resected specimen to the incidence of tuberculous complications is shown in Figure 2. A high tuberculous complication rate existed in instances where acid-fast bacilli could be demonstrated in the preoperative sputum or the resected specimen. The incidence of tuberculous complications in the 76 patients with positive preoperative sputum was 24 per cent. This contrasts with a 6 per cent incidence in the 189 patients with negative preoperative sputum. However, the greatest correlation of tuberculous complications with positive bacteriologic status exists in the case of cultures from the resected specimens.

The incidence of complications and deaths as related to preoperative pulmonary functions studies can be seen in Table 6. The morbidity and mortality were greater in those patients with a vital capacity or a maximum breathing capacity or less than 60 per cent of normal.

The common postoperative complications were analyzed in detail. Bronchopleural fistulae were encountered following three types of pulmonary resection: segmental resection, lobectomy and lobectomy plus partial lobectomy (Table 7). Ten of the 18 fistulae occurred in patients undergoing resections of a segment; thus of the 65 undergoing resection of a segment, 15 per cent developed postoperative bronchopleural fistula. Eight (4 per cent) of the 203 patients undergoing resections not involving removal of a segment had this complication. The results of treatment of bronchopleural fistulae are given in Table 7. Treatment by tube drainage and suction resulted in closure of the fistula in two or seven cases. Thoracoplasty resulted in closure of the fistula in six of the eight cases in which it was used as the definitive treatment. Direct suture of the fistula, alone or in conjunction with thoracoplasty, succeeded in two of three instances. It must be noted that every patient received a trial of tube drainage before other procedures were employed.

Of the six patients with postoperative tuberculous spread, two were controlled with drug therapy and two died 21 to 60 days following the resection. The other two had bronchopleural fistulae in addition to tuber-

TABLE 11—PHYSICAL ACTIVITY AND GAINFUL EMPLOYMENT IN THE FOLLOW-UP PERIOD

Daily Activity	1 Year	2 Years	3 Years	4 Years	5 Years
Working or in School Up Full Time*	15 } (22 per cent) 39 }	85 } (83 per cent) 43 }	84 } (96 per cent) 16 }	41 } (96 per cent) 4 }	7 } (100 per cent) 1 }
Up 6 hrs. to Full Time	92	24	3	2	0
Up Less than 6 hrs.	52	2	1	0	0

*Not known in some patients whether working or in school.

culous spread; the combination of drug therapy and thoracoplasty resulted in control of the spread and closure of the fistula in both instances. Of the five pleural space problems (without bronchopleural fistula) four required thoracoplasty to close the space and the fifth responded well to tube drainage alone. Hemothorax in the immediate postoperative period was encountered in seven patients. Prompt thoracotomy to control bleeding was required in four instances. Two were treated by tube drainage and proteolytic enzyme instillations. The seventh was treated by 24 blood transfusions, tube drainage and a delayed decortication. All seven made uneventful recovery.

Table 8 summarizes the results of treatment in the common major complications. Hemothorax and pleural space problems uniformly responded to treatment. The so-called tuberculous complications (bronchopleural fistula, empyema and spread) responded to treatment in only 60 to 66 per cent of the cases and one-half of those not responding to treatment ultimately died.

There were 16 patients who had two pulmonary resections during the period of this study. Twelve underwent bilateral resection within less than a ten month period; usually the time lapse between the two resections was six months. There were two major postoperative complications following the second resection: one a bronchopleural fistula that closed with treatment and the other died of severe respiratory insufficiency. Thus, of the 12 undergoing bilateral resection, 11 obtained an excellent result. In the other four instances the second resection was ipsilateral and was required because the first resection failed to produce a good result. There were two major complications; both were bronchopleural fistulae.

In addition to the 16 patients having two resections during the period of this study there were two others who had previous resection in another hospital three to ten years prior to the resection recorded in this series. Both of them had major complications, one was death due to respiratory insufficiency and other bronchopleural fistula that closed with treatment. Thus the 18 who underwent two resections accounted for seven of the major postoperative complications (13 per cent of the total of 55 complications) and two deaths (18 per cent of the 11 deaths).

TABLE 12—CUMULATIVE POST-RESECTION YEARLY FOLLOW-UP OF TUBERCULOUS ACTIVITY

	Postoperative* Period	1 Year	2 Years	3 Years	4 Years	5 Years
Inactive	187	183	160	110	47	7
(Died Inactive)			(1)		(1)	
Sputum Pos. × 1 or 2†	27	10	2	0	0	0
Active**	27	9	3	0	0	0
(Died Active)		(1)	(2)	(1)		
Lost to Follow-up	0	38	72	48	27	4
Eligible for Follow-up	241	241	240	159	75	11

*While still in hospital.

†Without other evidence of activity.

**Tuberculous empyema or BPF without other evidence of activity included in this group.

Postoperative Hospital Status

In the postoperative period, the patients were maintained on bed rest, antituberculosis drugs and general supportive measures. Most of them remained in the hospital for at least six months. The results of monthly postoperative sputum examinations are recorded in Table 9. Of the 238 patients available for this analysis 190 remained consistently negative. In 30 an occasional positive sputum (one or two) was encountered, while in 18 more than two positive sputa were obtained.

Pulmonary function studies were performed preoperatively and postoperatively in a significant number of patients; these studies are presented graphically in Figures 3 and 4. There were a significant number of patients in which maximum breathing capacity improved following pulmonary resection. In contrast, vital capacity improved following resection in only a small number. It is of interest that in the majority of patients the postoperative results were within plus or minus 10 per cent of the preoperative values; this was true for both tests.

Followup Studies

At the time of this report, all surviving patients are at least two years postoperative. During the first year after discharge from the hospital, patients were generally followed in the out-patient department of the Middle Tennessee Tuberculosis Hospital. Thereafter they were usually followed by their local county health department.

Antituberculosis drug therapy was generally continued until each patient had received two years of continuous treatment. Any one with evidence of continued tuberculous activity was treated for a longer period. Table 10 records the experience with postoperative drug therapy during the follow-up period. At the end of one year 87 per cent were still on drugs. This contrasts with only 12 per cent still on drugs after four years.

In Table 11 the daily physical activity of the patients with each year of follow-up is presented. This table gives an index to the usefulness of resective therapy as regards returning patients to productive, active lives. Beginning at the one year follow-up 22 per cent had returned to full activity and this increased to 83 per cent at the second year. Virtually 100 per cent had been restored to normal life before three years had passed.

Finally, Table 12 presents the follow-up studies in relation to tuberculous activity. It is of interest that only four patients died as a result of active pulmonary tuberculosis; two others died of causes unrelated to tuberculosis. A small number had evidence of tuberculous activity during the first one or two years following resection. Since then all available for follow-up have remained consistently inactive. Of the four dying of active tuberculosis during the follow-up period, three had developed persistent bronchopleural fistula following resection. There were 11 who were sputum negative at the time of discharge from the hospital and subsequently had positive sputum. Nine of these were only isolated instances of one or two positive sputa; the other two had more than two positive sputa and were considered to have active tuberculosis. Thus there were two in a total of 537 patient-years of follow-up who relapsed.

Discussion

This study provides further evidence that pulmonary resection can be performed in the treatment of pulmonary tuberculosis with an acceptable morbidity and mortality rate and reasonable expectation of an excellent result. It is not really possible to isolate resectional therapy in pulmonary tuberculosis from the other treatment that a patient receives (*i.e.*, drugs, bed rest, etc.). The effectiveness of drug therapy has been largely responsible for the feasibility of pulmonary resection. The primary role of resective therapy is to remove residual foci of tuberculosis after maximum benefit has been obtained from drug therapy, bed rest and other general supportive measures. If it can be shown that following pulmonary resection for tuberculosis the relapse rate is reduced to a minimum, the real value of resective therapy will have been established. In the present study only two patients had relapse during the follow-up period; this was two patients in a total of 537 patient follow-up years.

Pyrazinamide (PZA) coverage during the operative period proved effective in prevention of tuberculous postoperative complications in the present study. The incidence of tuberculous spread and tuberculous empyema were reduced to zero in the PZA treated patients.

There are certain factors which predispose to an increased morbidity and mortality following pulmonary resection for tuberculosis. It is often difficult, if not impossible, to designate a single critical factor as being responsible. In this study those in the older age groups sustained a higher incidence of complications and deaths. The male patients fared less well than the female; this was at least partly due to advanced age in the male group. The complication rate was equal in the Negro and white patients, but the Negro death rate was significantly higher than the white. This was partly due to the fact that pneumonectomy was more common in the Negro. Extent of resection played an important role in the incidence of complications and deaths; complications were three times as common and deaths two times as common in patients undergoing more than a lobectomy as in patients undergoing resection of a lobe or less. Duration of the disease process was another important factor; complications and deaths were twice as common in those with history of pulmonary tuberculosis of more than two years' duration. Positive sputum at the time of operation greatly increased the hazard of a postoperative complication or death, yet these patients probably stood to gain more from surgery than the sputum negative group. Grossly impaired pulmonary function clearly predisposed to postoperative complications and increased death rate. Patients undergoing two resections sustained an increased morbidity and mortality rate, but once again these patients clearly had more to gain.

The usefulness of pulmonary resection as an adjuvant in the treatment of tuberculosis is emphasized by the follow-up studies. Only four went on to die of tuberculosis and only two changed from inactive to active tuberculosis. All followed more than two years have remained inactive. By the second year they had returned to full and active life in 83 per cent of the cases.

SUMMARY

The experience with 268 consecutive pulmonary resections for proved pulmonary tuberculosis at the Middle Tennessee Tuberculosis Hospital has been presented. They were performed on 252 patients. There were 11 operative deaths (4 per cent), the majority of which occurred in the elderly patients with extensive disease and in whom extensive resections were performed.

Major postoperative complications occurred in 47 (17 per cent). Bronchopleural fistula occurred in 18 (7 per cent). Segmental resection was most commonly complicated by bronchopleural fistula (15 per cent), whereas, in the other types of resection bronchopleural fistula occurred in 4 per cent of patients.

Pyrazinamide therapy during the operative period proved effective in the prevention of tuberculous complications.

In the follow-up period, only four patients died of tuberculosis and only two have changed from inactive to active tuberculosis status. At the end of the two-year follow-up period, 83 per cent of the cases had returned to full and active life.

RESUMEN

Se representan los resultados de la experiencia obtenida de 268 resecciones pulmonares consecutivas en el Hospital de Tuberculosis de Middle Tennessee .

Se llevaron a cabo en 252 enfermos. Hubo 11 muertes operatorias (4 por ciento); la mayoría de esas muertes ocurrieron en personas ancianas con enfermedad extensa y en las que se hicieron amplias resecciones.

Las complicaciones mayores ocurrieron en 47 (17 por ciento) Se observo fistula broncopleural en 18 (7 por ciento). La resección segmentaria fue la que se complicó mas de fistula broncopleural (15 por ciento) en tanto que en las otras formas de resección la fistula broncopleural se vió en 4 por ciento de los enfermos.

La pirazinamida usada en el período postoperatorio demostró ser eficaz en la prevensión de las complicaciones tuberculosas.

En el período de seguimiento solo cuatro enfermos murieron de tuberculosis y solo dos regresaron a la actividad de la enfermedad despues de ser inactivos. Al fin de la observación por dos años, 83 por ciento de los casos han regresado a una vida activa completa.

RESUMÉ

L'auteur présente l'expérience qu'il a acquise après 268 résections pulmonaires pour tuberculose pulmonaire pratiqués dans l'Hôpital pour tuberculeux du Moyen Tennessee. Elles furent pratiquées sur 252 malades. Il y eut 11 décès opératoires (4%); la majorité d'entre eux survinrent chez des malades très âgés atteints d'affections étendues, et chez lesquels de larges résections ont été pratiquées.

Des complications post-opératoires majeures survinrent chez 47 malades (17%). Des fistules bronchopleurales survinrent chez 18 (7%). C'est dans la résection segmentaire que survint le plus habituellement les fistules bronchopleurales (15%) tandis que dans les autres types de résection, les fistules bronchopleurales n'étaient notées que chez 4% des malades.

Le traitement par la pyrazinamide pendant la période opératoire prouva son efficacité dans la prévention des complications tuberculeuses.

Pendant la période de surveillance, quatre malades seulement moururent de tuberculose, et deux seulement modifièrent leur condition de tuberculose inactive en évolutive. A la fin de deux années de surveillance, 83% des cas étaient rendus à une vie normale et active.

ZUSAMMENFASSUNG

Bericht über die Erfahrungen bei 268 aufeinanderfolgenden Lungenresektionen wegen erwiesener Lungentuberkulose aus dem Middle-Tennessee-Tuberkulosekrankenhaus. Sie wurden an 252 Kranken vorgenommen. Es ergaben sich 11 operative Todesfälle (4%); die Mehrzahl von ihnen ereignete sich bei den älteren Kranken mit ausgedehnten Befunden und bei denen weitgehende Resektionen ausgeführt worden waren.

Größere postoperative Komplikationen traten bei 47 (17%) der Kranken auf. Bronchopleurale Fisteln traten bei 18 (7%) Kranken ein. Die Segmentresektion war besonders häufig durch eine bronchopleurale Fistel kompliziert (15%), während bei den anderen Formen von Resektion bronchopleurale Fisteln nur bei 4% der Kranken sich entwickelten. Behandlung mit Pyrazinamid während der Operationszeit erwies sich als wirksam zur Verhütung tuberkulöser Komplikationen.

Während der Nachbeobachtungszeit starben nur 4 Kranke an Tuberkulose und nur bei 2 Kranken entwickelte sich aus dem inaktiven wieder ein aktiver tuberkulöser Befund. Am Ende der zweijährigen Nachbeobachtungszeit hatten 83% der Fälle ihre normale und aktive Lebensführung wieder aufgenommen.

TREATMENT OF TROPICAL EOSINOPHILIA

Diethylcarbamazine in single oral dose of 15 to 16 mg. per kg. body weight has been tried in 30 cases of tropical eosinophilia with gratifying results. The results of the present dose schedule compare favorably with those of parenteral (two injections — 6 to 8 mg./kg. body weight each on alternate days) and of seven-day oral therapy (8-10 mg./kg. body weight daily) already reported by the authors. No severe toxic reactions were observed. Minor untoward reactions were few and transitory.

Bhargava, H. S., Choubey, B. S., and Chouhan, S. S.: "Treatment of Tropical Eosinophilia with Diethycarbamazine," *J. Assoc. Phys. India*, 9:227, 1961.

MYOCARDIAL CONTRACTILE FORCE

The effects of five sympathomimetic amines on myocardial contractile force were determined with the Walton-Brodie strain-gage arch in 16 patients undergoing operations for congenital heart disease. Equal doses of norepinephrine and epinephrine produced almost identical increments in myocardial contractile force; equipressor doses of methoxamine resulted in little or no change in the force of contraction. Mephentermine and metarminor produced increments in myocardial contractile force similar to those following norepinephrine administration but the duration of action was longer. The results of these studies indicate there are no qualitative differences in the actions of these amines on cardiac contractile force of dog and man and provide a basis for the rational clinical use of these agents.

Goldberg, L. I., Bloodwell, R. D., Braunwald, E., and Morrow, A. G.: "Direct Effects of Norepinephrine, Epinephrine, and Methoxamine on Myocardial Contractile Force in Man," *Circulation*, 22:1125, 1960.

Massive Pulmonary Cavitary Bleeding*

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Massive hemorrhage is a serious complication of pulmonary cavitation and may result in death.[1,2,6,7] Some patients die of immediate exsanguination or suffocation leaving inadequate time for surgical intervention. The remaining group of patients with massive cavitary bleeding may be salvaged by operation if the site of bleeding can be localized early.

The source of bleeding in pulmonary cavities may be a pulmonary arterial aneurysm as first described by Fearn (1841).[4] Rasmussen[7] made a great contribution to the knowledge of such bleeding by careful anatomic studies demonstrating the presence of pulmonary arterial aneurysm in the wall of tuberculous cavities in 11 patients. Controversy exists, however, as to the exact type of lesion to be designated as Rasmussen's aneurysm. This is due in part to the fact that the demonstration of these aneurysms is often difficult and requires special pathologic technics and extreme diligence.[6] For this reason and because Rasmussen's aneurysms are the most common cause of pulmonary hemorrhage in the presence of cavitation, some authors[6] suggest that all cavitary bleeding be considered as Rasmussen's aneurysm. We prefer to acknowledge Rasmussen's contribution regarding this entity, but to refer to this group of lesions as cavitary bleeding.

FIGURE 1

FIGURE 2

FIGURE 1 (Case 1): Rather circumscribed density in the left upper lung field appears to contain numerous small cavities. This actually represents for the most part a large blood-filled cavity and the "infiltration" in the lingula and left lower lobe is largely aspirated blood. FIGURE 2 (Case 1): A large portion of the blood has evacuated itself revealing a single cavity. The density in the cavity represents blood which is probably clotted.

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Other conditions are known to cause hemorrhage in patients with pulmonary cavities. These include acute tracheobronchial disease, erosion of a pulmonary vessel by enlarged lymph nodes,[2] coagulation deficiencies and increased permeability of the vessel walls. An unusual cause of cavitary bleeding is erosion of the cavity wall by cavernolithiasis as described by Cooley.[3]

Recently, two cases of massive cavitary bleeding have served to focus our attention on this entity. These demonstrate the seriousness of the problem and emphasize the importance of proper diagnosis and immediate surgical intervention.

Case Reports

Case 1: J. W. H., a 42 year-old chronically ill white man, entered the hospital on September 9, 1958, with fever, left chest pain, and productive cough of four days' duration. His temperature was 101°F., and respirations 24. Examination of the chest showed numerous rales over the left mid-lung field with bronchial breath sounds. The liver edge was palpable 4 cm. below the right costal margin. Examination of the blood revealed a white cell count of 7,650 and a hemoglobin of 8.8 gm. The hematocrit was 28 vol. per cent.

Chest roentgenograms (Fig. 1) revealed a rather circumscribed area of infiltration in the left upper lung field. The primary involvement measured 10 cm. in diameter and appeared riddled with small cavities with extension into the lingula and lower lobe. Nine days later, a repeat roentgenogram (Fig. 2) revealed a huge, partially emptied cavity within the previously noted consolidation. A solid mass was seen within the cavity and the density in the lingula had increased.

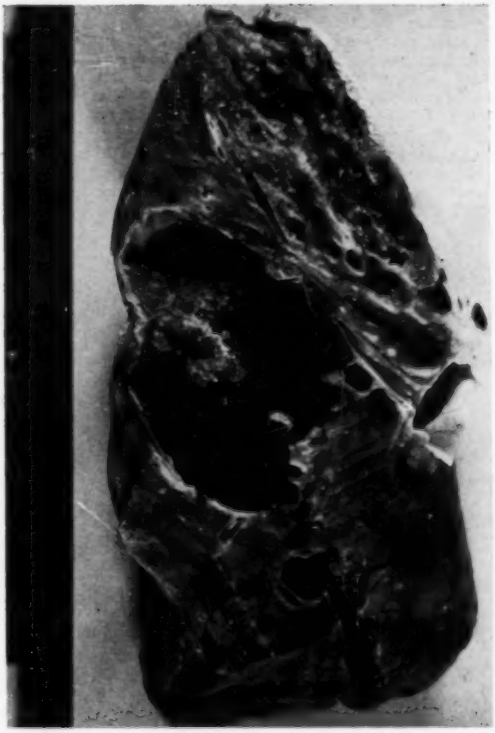

FIGURE 3 (Case 1): Section through the left lung showing the huge blood-containing cavity.

Sputum smear was negative for tubercle bacilli and pyogenic slides revealed a pure culture of staphylococci, sensitive to chlortetracycline (Aureomycin), tetracycline (Archromycin), streptomycin and kanamycin. Treatment with tetracycline (Achromycin) was begun and he was given three pints of blood.

Because of the possibility of active tuberculosis, transfer to another hospital was recommended. The day prior to transfer, he noted bloodstreaked sputum for the first time. Thirty minutes after readmission to the hospital, he experienced a massive pulmonary hemorrhage and died in five minutes.

Necropsy revealed a large abscess in the superior portion of the left lower lobe filled with clotted blood (Fig. 3). A branch of the pulmonary artery measuring 6 mm. in diameter was seen extending across the cavity wall, probably representing the source of bleeding. The entire tracheobronchial tree was also filled with blood. Smears taken from the abscess showed Gram-positive cocci.

This case represents an example of massive, fatal hemorrhage with minimal warning symptoms. On initial admission, his hemoglobin was only 8.8 gm. per cent suggesting blood loss, although he denied hemoptysis. Streaking of sputum became obvious one day prior to entry, but was hardly of the magnitude that might suggest impending disaster. This case indicates the potential danger of sudden exsanguination from a residual abscess with cavity.

Case 2: G. H. S., a 41 year-old white man, entered the hospital on January 8, 1959, because of hemoptysis. He was known to have active tuberculosis for which he had been hospitalized during the two previous years. In July, 1958, he left the hospital against medical advice. He continued to experience blood-streaked sputum and developed severe hemoptysis immediately before admission. Roentgenograms (Fig. 4) revealed active tuberculous infiltration bilaterally with a large cavity in the right midlung field. A smaller cavity was seen in the left upper lobe. Sputum smears and cultures were positive for tubercle bacilli and he was started on sodium PAS, 15 gm., pyridoxine, 25 mg. and isoniazid, 600 mg. daily.

He continued to experience intermittent hemoptysis productive of 200 to 300 cc. of blood daily. On February 23, 1959, pneumoperitoneum was induced with temporary improvement, but after one week, hemoptysis recurred requiring blood transfusions. Despite active bleeding, bronchoscopy was performed on March 20, 1959, revealing acute endobronchial disease in the right main stem bronchus, although no fresh bleeding point could be visualized. The left main bronchus and left upper lobe orifice appeared essentially normal.

Roentgenographic changes occurring serially after admission were of interest. On March 2, the large cavity which was apparent on admission in the superior segment of the right lower lobe had enlarged and contained a rounded mass (Fig. 5) with an

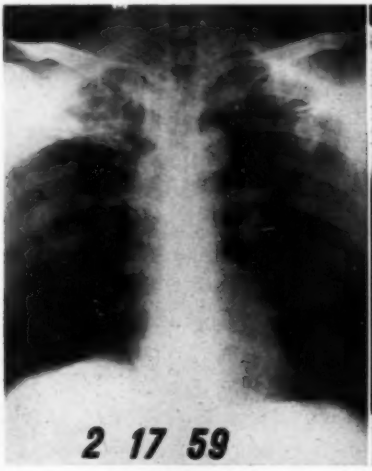

FIGURE 4

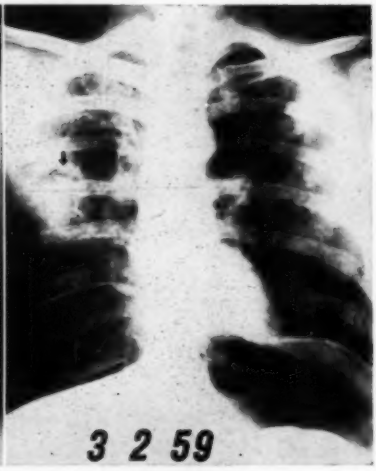

FIGURE 5

FIGURE 4 (Case 2): A large cavity in the apical segment of the right lower lobe is shown. A second smaller cavity can be seen in the left upper lobe with infiltration in both upper lobes. FIGURE 5 (Case 2): The cavity has become filled with blood and there is air above it forming the "halo" sign. Pneumoperitoneum has been induced.

overlying air cap. By March 13, the cavity was completely filled with the mass (Fig. 6) which later proved to be blood.

Bronchoscopic and radiographic findings suggested that he was bleeding from the large cavity on the right. Because of the presence of bilateral open cavities and active endobronchial disease, resection was temporarily postponed. However, pulmonary hemorrhages became progressively more severe in spite of conservative therapy and on March 26, 1959, right thoracotomy was carried out with resection of the superior segment of the right lower lobe. The specimen was found to contain a large cavity measuring 10 cm. in diameter and filled with clotted blood. A trabeculation was seen bridging the cavity which was thought to represent a branch of the pulmonary artery. Upon microscopic section, however, this was found to be a fibrous cord. Careful inspection of the wall of the cavity revealed numerous areas of granulation tissue filled with dilated capillaries which were probably responsible for the intense blood loss. Following surgery, the patient developed a bronchopleural fistula which closed with conservative measures. Isoniazid and PAS therapy has been continued and there has been no further bleeding (Fig. 7).

This patient was fortunate not to have exsanguinated or suffocated before his lesion was removed surgically. Once it became obvious that conservative measures were ineffective in controlling the pulmonary hemorrhage, surgery became mandatory. The main preoperative problem was the localization of the site of hemorrhage in the presence of bilateral cavitary disease. Although at the time we strongly suspected that the bleeding was from the cavity on the right, a review of the roentgenograms of the chest now reveals the changing appearance of the lesion and the characteristic "halo" effect, both suggesting a blood-filled cavity. This should have made it possible to proceed with surgical intervention on the right without hesitation.

Discussion

Early authors, discussing the problem of severe bleeding associated with cavitation, emphasize its occurrence in tuberculous patients. Auerbach,[1] in reviewing necropsies of 1,114 cases of tuberculosis, found 45 cases of fatal pulmonary aneurysms. Plessinger[4] reported on 49 tuberculous patients dying of massive pulmonary hemorrhage in whom it was possible to demonstrate a Rasmussen aneurysm in 29. Both authors indicated the tendency for these lesions to occur in association with chronic rather than acute lesions. Non-tuberculous cavities may also cause massive pulmonary bleeding as demonstrated by Case 1, and with the development of antibiotic resistant strain of bacteria, such lesions may become more prevalent. Furthermore, neoplasms undergoing central necrosis and cavity formation may be associated with severe bleeding.

The clinical picture prior to a massive cavitary hemorrhage is quite variable. In reporting 49 fatal cases of severe pulmonary bleeding, Plessinger[4] found that 26 patients had no previous hemoptysis and seven had experienced only one episode. This would indicate that in patients having a warning hemorrhage, as in Case 1, surgical intervention should be considered, especially when the bleeding can be localized to a chronic cavity. Occasionally, patients will be able to state from which lung

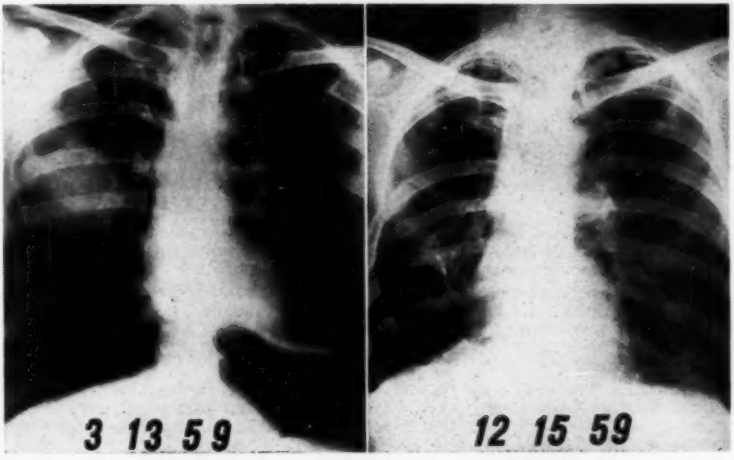

FIGURE 6 FIGURE 7

FIGURE 6 (Case 2): The cavity has become distended with blood resulting in further enlargement. FIGURE 7 (Case 2): Follow-up film made approximately one year after surgery.

the blood is arising. Physical examination during the active phase of bleeding will often reveal localized gurgling rales or rhonchi overlying the involved lobe or segment.

Appriopriate roentgenographic studies contribute most to the diagnosis and localization of this lesion. A cavity is visualized with radiographic evidence of intracavitary or intrapulmonary bleeding. Intracavitary bleeding is manifested by the appearance of fluid levels or the accumulation of a homogeneous radiopaque density in the cavity. The latter may have the appearance of a "halo" formed by an air cap lying above the blood density (Fig. 5). This may progress to distention with bulging of the cavity walls (Fig. 6). The roentgenographic manifestations of intrapulmonary hemorrahge varies considerably depending upon the amount of bleeding. It may be characterized by indistinct nodules, linear densities, hazy opacities, or dense masses with indistinct or sharply defined borders.

Bronchoscopy at the time of active bleeding is a valuable procedure when not contraindicated by the critical condition of the patient. If bronchoscopy is delayed, the opportunity to localize the site of hemorrhage may be lost. It should be recognized, however, that massive hemorrhage may suddenly occur during bronchoscopy. Hamilton[5] has reported such a case in which exsanguination was prevented by rapid intubation of the opposite bronchus and emergency thoracotomy. The decision to intervene surgically should be based upon a careful clinical appraisal by both the internist and surgeon. In general, the presence of severe hemorrhage with roentgenographic demonstration of a bleeding cavity, justifies prompt surgery. The procedure of choice is removal of the cavity, usually by segmental resection or lobectomy. Following its removal, the cavity should be opened and carefully inspected for the presence of blood. If none is found, another source of bleeding should be considered. The possibility of a neoplastic cavity should be kept in mind and frozen sections made of any suspicious lesion.

SUMMARY

1. Two cases of massive hemorrhage within pulmonary cavities are reported, one presenting as a nontuberculous lung abscess which terminated fatally and the other a tuberculous cavity successfully resected.

2. Although the clinical findings are often helpful, the diagnosis and localization of the lesion is usually made by radiographic techniques. Evidence of hemorrhage arising from a cavity may be found in the changing appearance of the lesion with the development of a "halo" formed by an air cap overlying the blood density.

3. With severe bleeding and radiographic evidence of its origin from a pulmonary cavity, prompt surgical intervention is indicated. The chief objective of the surgery is the removal of the bleeding cavity and this should be accomplished with a minimal resection.

RESUMEN

1. Se presentan dos casos de hemorragia voluminosa dentro de cavidades pulmonares, uno en absceso pulmonar que terminó fatalmente y el otro en una cavidad tuberculosa resecada con éxito.

2. Aunque los hallazgos clinicos son utiles, a menudo el diagnóstico y la localización de la lesión se obtienen por la técnica radiológica. La evidencia de hemorragia emanado de una cavidad puede encontrarse en la apariencia cambiante de la lesión con la aparición de un "halo" formado por la cámara de aire sobre la densidad de la sangre.

3. Ante la hemorragia grave y la evidencia radiológica de su orígen la inmediata intervención está indicada. El principal objetivo es la supresión de la cavidad sangrante y esto debe llevarse a cabo con una resección mínima.

RESUMÉ

1. L'auteur présente deux cas d'hémorragie massive dans des cavités pulmonaires, dans un cas il s'agissait d'un abcès pulmonaire non tuberculeux dont l'issue fut fatale, et dans l'autre d'une cavité tuberculeuse opérée avec succès.

2. Bien que les constatations cliniques soient souvent précieuses, ce sont habituellement les radiographies qui précisent le diagnostic et le siège de la lésion. La preuve de l'hémorragie provenant d'une cavité peut être offerte par le changement d'apparence de la lésion, avec développement d'un "halo" formé par le croissant d'air surmontant l'opacité sanguine.

3. En présence d'un saignement grave et de la preuve radiographique de son origine à partir d'une cavité pulmonaire, une intervention chirurgicale rapide est indiquée. Le principal objectif de la chirurgie est l'exérèse de la cavité hémorragique et ceci devrait être pratiqué avec une résection a minima.

ZUSAMMENFASSUNG

1. Es wird über 2 Fälle massiver Blutungen im Inneren von pulmonalen Kavernen berichtet, von denen der eine einen nicht-tuberkulösen Lungenabszess darstellte mit tödlichem Ausgang und der andere eine mit Erfolg resezierte tuberkulöse Kaverne war.

2. Obwohl die klinischen Befunde oft von Nutzen sind, wird die Diagnose und Lokalisation des Befundes gewöhnlich aufgrund der röntgenologischen Untersuchungsmethoden gestellt. Ein Anhaltspunkt für eine voneiner Kaverne ausgehende Blutung läßt sich gewinnen aufgrund des wechselneen Aussehens des Herde mit Entwicklung eines "Hofes," der durch eine den dichten Blutschatten überlagernde Luftkappe gebildet wird.

3. Mit der schweren Blutung und dem röntgenologischen Befund ihres Ursprungs aus einer pulmonalen Kaverne, ist sofortiges chirurgisches Eingreifen indiziert. Das Hauptziel für den Chirurgen besteht in der Entfernung der blutenden Kaverne, und dies sollte in Form einer minimalen Resektion geschehen.

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RESPIRATORY EFFECTS OF RESISTANCE TO BREATHING

The respiratory effects of resistance to breathing have been studied in 28 patients anesthetized for routine surgery, but permitted to breathe spontaneously. Resistances were imposed for periods of 2-7 minutes and ventilation was then compared with the control periods of unobstructed breathing. The passage of inspired and/or expired gas through a water trip (threshold resistor) produced less than the expected reduction in ventilation since there was an immediate, presumably reflex, augmentation of the developed inspiratory tension. Thereafter, there was a further increase in ventilation probably due to CO_2 retention — full compensation being achieved in 2-3 minutes. There was a wide scatter in the ability of patients to compensate. Some patients attained a minute volume close to the control value against as much as 17 cm. water, while the worst response was apnea at 12 cm. water with proportionate reduction against lower pressures. In the present study, the ability to compensate was not found to be impaired by halothane, small doses of relaxants, old age or early emphysema.

Nunn, J. F., and Ezi-Ashi, T. I.: "The Respiratory Effects of Resistance to Breathing in Anesthetized Man," *Anesthesiol.*, 22:174, 1961.

TREATMENT OF TUBERCULOUS PLEURITIS

In this article, the authors review the actual status of the treatment of tuberculous pleuritis and discuss the introduction of corticosteroids as a mode of therapy. Sixty secondary and 20 primary cases of tuberculous pleuritis seen at the tuberculosis clinic of the University of Istanbul between 1952 and 1960 are presented. These patients were all women and their age ranged from 11 to 70. Resorption time was estimated among these patients treated by antibiotics alone or in combination with corticosteroids. It was noticed that in patients treated by antibiotics alone, the minimum resorption time was three weeks and the maximum time was 18 weeks, the average being ten weeks. On the other hand, in patients where corticosteroids were combined as a means of treatment, the average resorption time was 6.5 weeks.

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Azygography in Bronchogenic Carcinoma

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The question of whether radical resection for bronchogenic carcinoma is possible may be answered beside numerous clinical examinations chiefly on the basis of diagnostic thoracotomy, because in initial stages of the disease, it is difficult, with other means, to establish the presence of metastases in lymph nodes and the pleura. As reviewed by Gibbon[3] *et al.*, thoracotomy rendered useful information in 13 to 71 per cent of 9,565 cases of bronchogenic carcinoma diagnosed by 18 surgeons, while extirpation was useful only in 5 to 39 per cent of the cases. In Ochsner's experience (1960) in 875 of his own cases, thoracotomy revealed useful information in 60 per cent while curative resection was possible only in 10 per cent. All these authors, with the best diagnostic procedures at their disposal, were faced in nearly half of the thoracotomized patients with a situation in which resection was not advisable. The findings of Brock[4] and Higginson[5] concerning radical operative procedures are much more disappointing. The latter found lymph node metastases in 64 per cent of 45 operated patients.

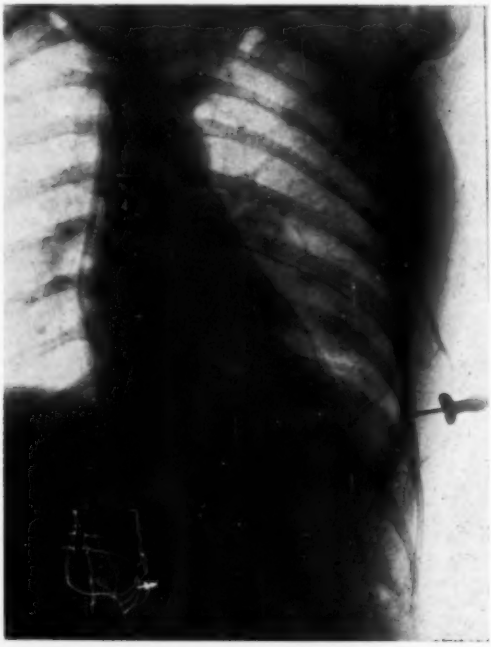

FIGURE 1: Tumor of the left lower lobe. Because of mediastinal metastases, the azygos vein (dotted line) and the hemiazygos are not visualized; the pericardial and parietal networks are well discernible.

*From the University Clinic for Chest Diseases, College of Medicine.

Examinations previous to operation can detect only metastases of larger dimensions in lymph nodes, because only these cause significant changes in nerves, veins and other structures of the surrounding region. Contralateral or distant metastases may remain unnoticed even at the time of thoracotomy. Azygographies performed on some of our patients with bronchogenic carcinoma presented unusual pictures thus evoking our interest.

Methods

Since the beginning of 1956, azygography has been performed at the Clinic for Chest Disease on 112 patients with proved bronchogenic carcinoma. Contrast substance** was injected under moderate pressure on the left or right side, in most cases in the eighth rib. Two x-ray films were taken, the first when two-thirds of the contrast substance was injected, the second when its total quantity was injected. The patients were kept in dorsal position. The tumor was localized in 57 in the right upper lobe, in 38 in the left upper lobe and in 17 cases in the lower lobes. The tumor was in close connection with the hilum of the lung in 93 cases, while in 19, it was situated in the pulmonary tissue without radiographically demonstrable connection with the mediastinum. Where the tumor's localization was central, the azygos vein was not visualized either

FIGURE 2: The azygos vein is not visualized in the roentgenogram; only its parietal ramification is discernible in the transcostal venogram.

**20 ml. of 70 per cent Urographin.

partially or totally in the roentgenogram. It was thus possible to demonstrate not only the lack of visualization of the azygos vein, but also the formation of collateral circulation of various degrees and extends, as well as its compensatory dislocation. These findings support the evidence of an organic obstruction of the azygos vein. As to peripheral tumors, of 19 cases only 5 presented normal appearance of the azygos vein. Three of these patients had metastases in lymph nodes detected by the surgeon during operation. Only palliative operation could be performed on these patients.

Those with azygographic evidence of the obstruction of the azygos vein and with the presence of collateral circulation were not considered suitable for surgery. Indications for operation were based on routine clinical examinations including thoracotomy and thoracoscopy. As a consequence of obstruction of the azygos vein, changes were observed also in the direction of blood flow. In most cases, it was into the inferior vena cava, in other cases, it was toward the contralateral axillary or innominate veins through the lateral thoracic and internal mammary veins. The obstruction of the azygos vein as seen in the roentgenograms was observed at different levels, but most frequently corresponding to the sixth or seventh vertebra. The well-delineated stump continued in the sinous thoracoabdominal section.

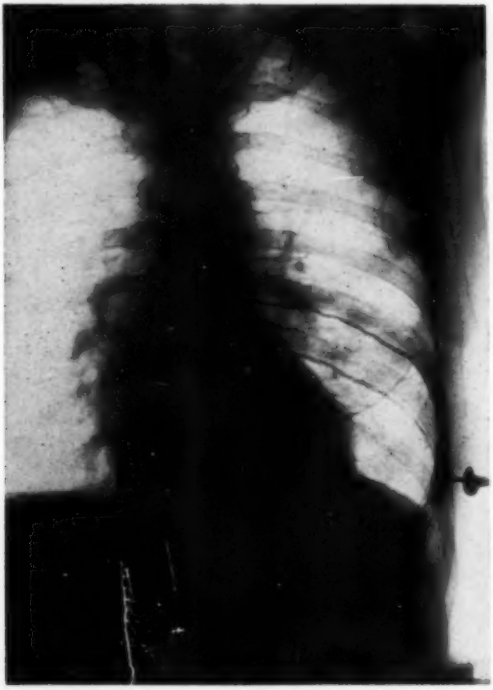

FIGURE 3: Azygogram in bronchogenic carcinoma of the left lower lobe. The azygos vein fails to appear in the azygogram (dotted line) because of the metastases in the dorsal lymph nodes. The hemiazygos and the veins of the chest wall are well visible.

Discussion

Rouviere[11] and Brock,[4] and later Kubik,[9] observed the regional lymph node system to surpass the homolateral localization with paratracheal extension under the bifurcation, often also into the contralateral paratracheal and paraesophageal regions. This observation pertains especially to the left lower lobe.

It has been known since Beck and Beattie's[2] investigation that especially paratracheally and in the dorsal parts of the mediastinum, numerous lymph nodes are surrounding the azygos vein. By meticulous necropsy, it was possible to demonstrate the presence of 64 nodes in this region. According to these two authors, radical resection for bronchogenic carcinoma should include the removal of about 50 mediastinal nodes. Of 112 cases, we have found in five radiographically demonstrable extension of the tumor of the left lower lobe into the right upper paratracheal mediastinal region.

According to Wegelin,[17] Walther[16] and Bányai,[1] in bronchogenic carcinoma early metastases are detectable in the regional lymph nodes in 63.5 to 93 per cent of the cases. In the light of these findings and supported by our own observations it is justifiable to call attention to the possible significance of preoperative radiographic exploration of the azygos vein which may be occluded by the surrounding lymph nodes. In case of obstruction of the azygos vein and the formation of a collateral circulation, the authors express their doubt of the usefulness of surgical intervention with the aim of palliation.

SUMMARY

Azygography performed on 112 patients suffering from proved bronchogenic carcinoma showed evidence of occlusion of the azygos vein in each instance of centrally localized tumors. Beside obstruction of the azygos vein, metastases were also observed in the contralateral mediastinal lymph nodes in hilar distribution. The harmless method of azygography can afford useful help in preoperative exploration of mediastinal metastases in bronchogenic carcinoma.

RESUMEN

La azigografía realizada en 112 enfermos que sufrían carcinoma broncogénico demostrado, manifestaron evidencias de oclusión de la vena azigos en cada caso de tumores localizados centralmente.

Aparte de la obstrucción de la vena azigos, se observaron también metástasis en los ganglios linfáticos contralaterales en su distribución hiliar. El método inofensivo de la azigografía puede ofrecer ayuda útil en la exploración preoperatoria de las metástasis mediastinales del carcinoma bronquiogénico.

RESUMÉ

Une azygographie pratiqués sur 112 malades souffrant de cancer bronchique diagnostiqué a montré l'existence d'une occlusion de la veine azygos dans chaque cas de tumeurs localisées. Outre l'obstruction de la veine azygos des métastases furent également observées dans les ganglions médiastinaux controlatéraux. La méthode inoffensive de l'azygographie peut apporter une aide efficace dans l'appréciation préopératoire des métastases médiastinales du cancer bronchique.

ZUSAMMENFASSUNG

Eine Azygographie bei 112 an bestätigtem Bronchialcarzinom leidenden Kranken ergab Anhaltspunkte für einen Verschluß der v.azygos bei allen Fällen von Tumoren mit zentralem Sitz. Abgesehen von dem Verschluß der v.azygos wurden Metastasen auch beobachtet im Bereich der kontralateralen mediastinalen Lymphknoten mit hilärer Verteilung. Die harmlose Methode der Azygographie kann nützliche Hilfe leisten bei der präoperativen Ermittlung mediastinaler Metastasen des Bronchialcarzinoms.

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THE BRONCHOSCOPIST VIEWS ASTHMA

In the normal tracheobronchial tree, the lumen becomes larger on inspiration and smaller on expiration. In the asthmatic patient, this alteration in caliber is exaggerated so that on expiration the lumen may almost be obliterated. This narrowing is not concentric, but is caused by approximation of the posterior and anterior walls, giving a scabbard-shaped lumen. We have had some patients who could obtain relief in their severe attacks only by bronchoscopy. In these cases, the endoscopic appearance as well as the relief obtained is dramatic. The membrane is thick and edematous and the mechanics of the expiratory dyspnea become clear as one watches the posterior wall mound forward and meet the anterior wall as the patient makes tremendous expiratory effort. An enormous amount of thick gelatinous secretion is trapped distal to these collapsing walls and increases the obstruction still more. As the bronchoscope props the walls apart and the aspirator removes the secretion, the patient is able to breathe again.

Van Loon, E. L.: "The Bronchoscopist Views Asthma," *Penn. Med. J.*, 64:49, 1961.

INCREASED TRANSRADIANCY OF ONE LUNG

The author reports cases recognized on clinical examination by diminished breath sounds over one lung and by decreased movements of the chest wall on the same side. X-ray examination shows increased transradiancy of the affected lung and diminished hilar and vascular shadows. Fluoroscopy reveals a picture similar to that of obstructive emphysema; there is diminished excursion of the affected lung and deviation of the mediastinum toward the normal side on expiration. Bronchoscopy and bronchography, however, reveal no evidence of obstruction in the major bronchi, but bronchography does reveal an abnormality of the peripheral bronchi, either of the whole lung or of one or more lobes. Pulmonary function studies characteristically reveal diminished ventilation and markedly diminished oxygen uptake in the affected lung or in one or more lobes. Angiograms show that the pulmonary artery is reduced in size. The whole vessel may be involved or only the lobar branches. This syndrome has been variously described as: abnormal transradiancy of one lung, increased transradiancy of one lung, unilateral pulmonary "emphysema," hypoplasia of the pulmonary artery and idiopathic unilateral hyperlucent lung.

Leahy, D. J.: "Increased Transradiancy of One Lung," *Brit. J. Dis. Chest*, 55:72, 1961.

The Surgical Treatment of Primary Malignant Lymphoma of the Lung*

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A search of the recent medical literature will reveal a resurgence of interest in primary malignant lymphoma of the lung.[1-9] According to Sternberg and associates,[10] 60 cases of primary pulmonary lymphoma had been reported in the literature up to 1959. Included in this number were the seven cases which formed the basis for their report. Of these, 39 were cases of lymphoma of the lymphocytic type, 14 of Hodgkin's disease, and seven of reticulum cell sarcoma.[10] Although this disease, which was first reported by Murchison[11] in 1870 and recognized as a clinical entity by Terplan[12] in 1922, is uncommon, recent emphasis that the lesion may remain localized for long periods has led to the concept that early surgical removal is not only feasible, but advisable in some instances.

As the fact that primary malignant lymphoma of the lung could be treated surgically has become accepted, the literature reporting the various results of treatment has included an increasing number of cases.[4,6,7,9,15-17] In few reported cases, however, is the follow-up period sufficiently long to indicate clearly whether or not the surgeon was able to alter the course of the disease. Five years have passed since Cooley, McDonald and Clagett[4] reported a series of nine cases of primary pulmonary lymphoma. A follow-up study of these patients and a report of experience with subsequent cases, therefore, were thought advisable.

Material and Methods

As a prelude to a clinicopathologic study of primary malignant lymphoma of the lung, a proper definition of conditions that form the basis for the assumption that the disease is primary in the lung is necessary. Accordingly for our study we decided that the condition first must be shown histologically by adequate biopsy to be a malignant lymphoma. To establish that the lymphoma is predominantly within the lung rather than a mediastinal structure requires direct examination, usually at thoracotomy. The procurement of a specimen that is definitely from a malignant lymphoma by either bronchoscopic or needle biopsy methods was not considered to be sufficient evidence that the process was primary in the lung. Our second condition, therefore, was an absence of evidence both at thoracotomy and in the case record that the malignant lymphoma in the lung was part of a disseminated process or that the lung was involved secondarily. Since lesions can be found in the lung in approxi-

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mately 40 per cent of the cases of disseminated lymphoma,[18] an isolated lesion in the lung per se does not identify the lung as the primary focus.

Even with these criteria, it may be difficult at times to tell even when the removed pulmonary tissue is examined in the pathology laboratory whether the disease started in the parenchyma of the lung or whether it started in adjacent lymphoid tissue and invaded the lung. If the bulk of the tumor is located within the parenchyma of the lung and appeared to invade hilar or mediastinal structures secondarily, it seemed to us reasonable to include the case in our discussion of primary malignant lymphoma of the lung. These then were the criteria which we used in the selection of cases.

From July, 1954, through July, 1959, ten patients whose cases have not been reported previously have met these criteria and have been treated surgically at the Mayo Clinic for primary malignant lymphoma of the lung. The clinical and laboratory records and the thoracic roentgenograms of these patients were examined (Figs. 1 to 4). Attention was paid to the symptoms that were present and instrumental in bringing the patient to the physician and to determining whether there was any evidence of lymphoma elsewhere in the body.

Bronchoscopic findings were reviewed for descriptions of any changes noted by the endoscopist. These observed aberrations varied from displacement of bronchial structures to actual visualization of the lesion in the bronchus. Reports of bronchial biopsies and cytologic studies for malignant cells in bronchial washings and sputa were tabulated, and the material was reviewed. Gross specimens (Fig. 5) which were available in all cases were examined along with the original microscopic slides, and additional slides were prepared from the specimens (Fig. 6 and 7).

Questionnaires requesting a statement concerning their health and a list of any additional treatments that they may have undergone were sent to each patient surviving the operation.

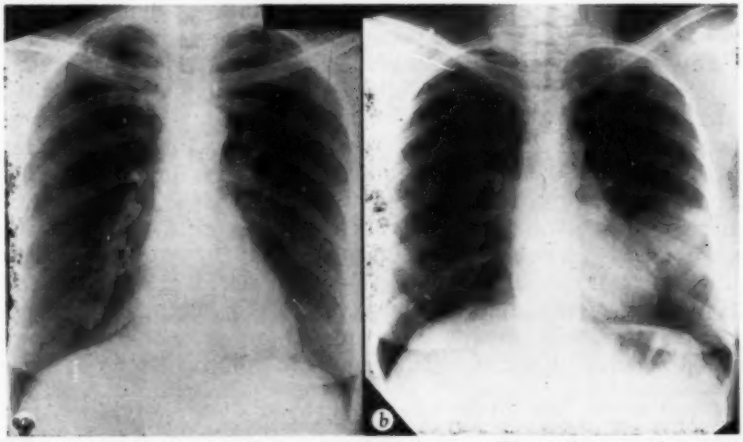

FIGURE 1: Malignant lymphoma, lymphocytic type. The various roentgenographic patterns presented by the lymphoma in our series (Figs. 1 to 4) should be compared. *a* (Case 1). Relatively well-localized coin-sized lesion in right lower part of the lung field in preoperative roentgenogram made August 14, 1959. *b* (Case 6). Poorly outlined infiltration may be noted in the left lower part of the lung field. The contrast between *a* and *b* is marked.

Report of Cases

Case 1—A 46-year-old housewife was seen at the clinic with complaints of dyspepsia and intolerance to fatty food; these were thought to be due to a nonfunctioning gallbladder. Roentgenograms of the thorax showed a well-defined, coin-sized lesion in the right lower lobe of the lung (Fig. 1*a*). Tomograms failed to show calcification in the lesion, and operation was advised. Hemograms and sedimentation rate were all within normal limits. Cholecystectomy was performed, and following this, the incision was extended into the right side of the thorax. A firm, round mass could be palpated deep in the lower lobe of the lung; therefore, a right lower lobectomy was performed. Pathologic examination disclosed a grayish-tan mass deep within the lobe which had infiltrated the parenchyma near a segmental bronchus. The tumor measured 2.5 by 2 by 2 cm. (Fig. 5*a*). In fresh frozen section, this was found to be a malignant lymphoma of lymphocytic type (Fig. 6*a*). Hilar nodes were negative for malignancy. The patient was dismissed from the hospital on the ninth postoperative day, made an uneventful recovery, and is well to date. No postoperative roentgen therapy was given because the lesion was small and excision alone was deemed adequate.

Case 2—A 60-year-old housewife came to the clinic in October, 1958, with the complaint of cough and dyspnea of two months' duration and wheezing in the right side of her thorax. The hemoglobin measured 11.9 gm. per 100 ml., and the leukocyte count was 4800 per cubic millimeter of blood. The sedimentation rate was 84 mm. in 1 hour (Westergren). On serologic examination, the Kahn test gave a 4+ reaction, and later studies indicated that this was a biologically false positive reaction. Roentgenograms of the thorax demonstrated unilateral emphysema on the right, which suggested obstruction of the right main bronchus, although no definite mass could be seen (Fig. 2*a*). Bronchoscopy, however, revealed a markedly strictured right intermediate bronchus. It was possible to view the right upper lobe bronchus with the right angle telescope, and this was almost completely occluded. A small mass of what appeared to be tumor tissue was seen in the inferior angle of the bronchus. This was removed, the tip of the bronchoscope was introduced through the stenotic region, and more tumor was seen in the right intermediate bronchus. The carina appeared normal, as did the left bronchial tree. The bronchial biopsy was considered compatible with a diagnosis of undifferentiated small cell malignant lesion, either a lymphocytic lymphoma or a small cell carcinoma. On October 18, 1958, thoracotomy was performed. The lung was emphysematous, distended and tense and could not be collapsed readily because of bronchial obstruction. A palpable mass in the right upper lobe extended deeply into the hilus, and several lymph nodes along the main bronchus appeared grossly neoplastic; this observation was confirmed by histologic examination. Right pneumonectomy was performed. Pathologic examination of the specimen showed an obstructive malignant lymphoma of lymphocytic type which circumferentially involved the major bronchi and extended submucosally into the right upper and middle

FIGURE 2: Malignant lymphoma, lymphocytic type. *a* (Case 2). Roentgenogram made after complete expiration. Obstructive emphysema is evident on the right without any apparent mass. Tumor was discovered at bronchoscopic examination. *b* (Case 5). Roentgenographic evidence of atelectasis in right lower part of the lung without any demonstrable discrete mass proximal to the collapsed lobe.

TABLE 1—PRIMARY MALIGNANT LYMPHOMA OF THE LUNG IN 10 PATIENTS TREATED SURGICALLY AT THE MAYO CLINIC: 1954 TO 1959 INCLUSIVE

Case	Age, yr. and sex	Symptoms	Duration, mo.	X-rays	Sedimentation rate, mm. in 1 hr.	Bronchoscopic examination	Lesion		Survival, mo.
							Extent and resection	Type	
1	46F	None		Nodule	15	Not done	Right lower lobe	Lymphocytic	5
2	60F	Dyspnea; cough; wheezing	2	Obstructive emphysema	84	+	Right lung	Lymphocytic	12
3	38M	None		Mass	7	+	Right lung	Lymphocytic	Died in hospital
4	42M	None Mass in x-rays Later: wheezing, cough	 36 24	Mass	47	Negative	Right upper lobe	Lymphocytic	26
5	50M	Cough; dyspnea; wheezing	2	Atelectasis	12	Negative	Right lower and middle lobes	Lymphocytic	40
6	43F	None Abnormal x-ray	 18	Infiltration	23	Not done	Left lung	Lymphocytic	6
7	4M	Fever; dyspnea	9	Pleural effusion; pulmonary infiltrate	39	Negative	Left lower lobe	Lymphocytic	Died in hospital
8	49M	Hemoptysis; pain	9	Cavity in mass	48	Negative	Right upper lobe	Hodgkin's	24*
9	70M	Cough; fever	2	Atelectasis	130	+	Left lung	Hodgkin's	Died in hospital
10	37M	Hemoptysis; fever; cough	About 1	Mass	42	+	Right middle and lower lobes	Reticulum cell	Late death

*Evidence of clinical recurrence.

lobe bronchi, with obstructive pneumonitis and emphysema distal to the lesion (Fig. 7*a*). After operation the patient was given roentgen therapy and treatment with nitrogen mustard.

At last report, one year following operation, she stated that her health was good.

Case 3—A 38-year-old priest came to the clinic in March, 1957, complaining of headache of three weeks' duration. His physician had found roentgenographic evidence of a mass in the thorax and had referred him for treatment. Laboratory work-up disclosed 13.2 gm. of hemoglobin per 100 ml., 8400 leukocytes and a sedimentation rate of 7 mm. in one hour. The differential count was normal. Roentgenographic examination again revealed a mass involving the right hilus (Fig. 3*a*). At bronchoscopy a tumor was seen protruding into the lower lobe bronchus. A specimen was removed and was interpreted as being an undifferentiated malignant neoplasm of a small cell type.

At exploration on March 4, 1957, a large mass the size of a fist was found in the hilus of the right lower lobe near the inferior pulmonary vein. Right pneumonectomy was performed. Several large nodes at the right hilus were removed but did not contain tumor. On pathologic examination the mass measuring 7.5 cm. involved the hilus and lower lobe bronchus and was microscopically a malignant lymphoma, lymphocytic type, with a prominent follicular component (Fig. 7*b*). One of the hilar nodes was involved by direct extension.

Unfortunately, on the day following the operation, the patient became increasingly more dyspneic and succumbed. Significant postmortem findings included a single 1.5-cm. nodule of lymphocytic lymphoma in the upper lobe of the left lung and bronchopneumonia with pulmonary edema.

Case 4—A 42-year-old policeman was first seen at the clinic in June, 1957. He had complained of wheezing and coughing for two years, and review of roentgenograms taken elsewhere revealed that a mass had been present in the right lung for three years.

Laboratory studies showed 12.7 gm. of hemoglobin, 4500 leukocytes and a sedimentation rate of 47 mm. in one hour (Westergren). The differential count was normal. Thoracic roentgenograms revealed a mass in the right lung at the hilus, but bronchoscopic examination was negative. A subsequent roentgenogram of the chest showed a questionable infiltration in the left pulmonary field.

At diagnostic thoracotomy performed on June 18, 1957, a large, firm tumor was found in the right upper lobe of the lung, which was removed by lobectomy. Pathologic examination disclosed a malignant lymphoma of lymphocytic type which measured 11 by 7 by 6 cm. and had infiltrated almost the entire upper lobe. Lymph nodes were not involved.

A course of roentgen therapy was given to both sides of the thorax subsequent to the operation, and the process in the left lung began to clear rapidly, so that eventually it was no longer evident. Twenty-six months following dismissal from the hospital no evidence of recurrence could be found.

Case 5—A 50-year-old farmer came to the clinic in January, 1956, complaining of cough and dyspnea of two months' duration. Seven months prior to these complaints he had noted the onset of expiratory wheezing. The value for hemoglobin was 13.2 gm. per 100 ml., the leukocyte count was 5800, and the differential count was normal.

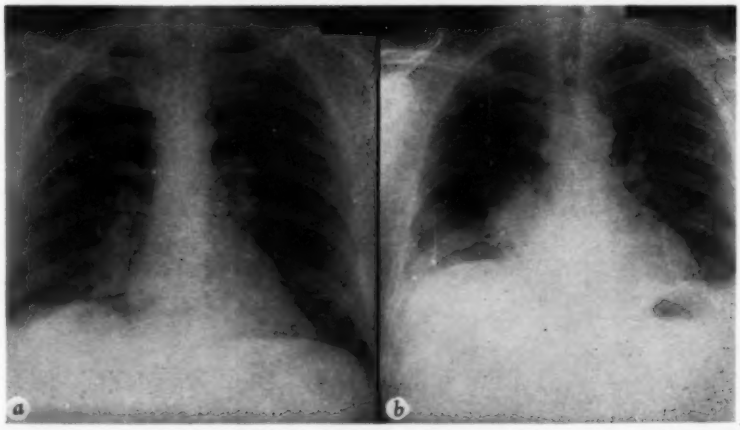

FIGURE 3: Malignant lymphomas, lymphocytic type. *a* (Case 3). The feathery appearance of the periphery of the tumor shadow in the right lower part of the lung is evident. This should be contrasted with *b*. *b* (Case 10). Reticulum cell type. A sharply outlined mass is seen in the right lower part of the lung.

TABLE 2—PRIMARY PULMONARY MALIGNANT LYMPHOMA IN NINE PATIENTS TREATED SURGICALLY AT THE MAYO CLINIC PRIOR TO 1954: CASES PREVIOUSLY REPORTED BY COOLEY AND ASSOCIATES[4]

Case	Age, yr. and sex	Symptoms	Duration, mo.	X-rays	Sedimentation rate, mm. in 1 hr.	Bronchoscopic examination	Lesion		Survival
							Extent and resection	Type	
11	47M	Cough; fever	6	Mass	29	+	Left upper lobe	Lymphocytic	7½ yr.
12	67F	Fever; hemoptysis	12	Mass and atelectasis	100	+	Right lung	Lymphocytic	Died in hospital
13	36F	Cough	36	Mass and atelectasis	35	+	Right lung	Lymphocytic	13 yr.
14	34F	Cough; fever; hemoptysis	3	Cavity	57	Not done	Left lung	Hodgkin's	5 yr.*
15	64F	Cough; dyspnea	9	Cavity	78	Negative	Left lung	Lymphocytic	Late death
16	59M	Cough	2	Mass and atelectasis	15	+	Inoperable	Reticulum cell	Late death
17	19F	Fever; hemoptysis	3	Cavity	86	+	Inoperable	Hodgkin's	Died in hospital
18	27F	Pain	1	Mass	73	Negative	Inoperable	Hodgkin's	4 mo.; lost to follow-up
19	29F	Cough; fever	3	Mass	78	+	Left lung	Hodgkin's	Late death

*Indicates clinical evidence of recurrence.

The sedimentation rate was 12 mm. per one hour. A roentgenogram of the thorax showed atelectasis of the right lower lobe without an apparent mass at the hilus (Fig. 2*b*). Bronchoscopy was not revealing, and cytologic studies for malignant cells were negative.

Right thoracotomy was done on January 21, 1956. Approximately 300 cc. of slightly brownish pleural fluid was removed, and the right lobe appeared indurated, completely airless and contracted. There was an absence of the fissure between the middle and lower lobes. Although initially an inflammatory process seemed likely, the right middle and lower lobes were removed because a neoplastic process could not be excluded. On pathologic examination, both lobes were diffusely infiltrated by a pinkish-tan malignant lymphoma of the lymphocytic type (Fig. 5*b*). The hilar nodes were not involved. The patient was given a course of x-ray therapy after operation, and when last seen in May, 1959, he was in good health.

Case 6—A 43-year-old housewife was referred here in February, 1958, because of an abnormal shadow found in her left lung in a routine thoracic roentgenogram. The results of the physical examination and laboratory studies were negative. Since a neoplasm of the lung could not be ruled out, operation was advised, but this was deferred by the patient. The lesion was followed by subsequent roentgenograms (Fig. 1*b*), and on July 24, 1959 had increased in size. The patient then consented to operation. Laboratory studies at this time showed 13.0 gm. of hemoglobin, 5400 leukocytes and a sedimentation rate of 23 mm. in one hour. Bronchoscopy was not performed.

At thoracotomy on July 28, 1959, the lesion in the lingula had extended into the anterior segment of the upper lobe and across the anterior basal segment of the lower lobe. To the surgeon, the shiny, heavy lung resembled an alveolar cell carcinoma. A specimen was removed and examination of fresh frozen sections showed a malignant lymphoma of the lymphocytic type; therefore, pneumonectomy was performed. Pathologic examination disclosed a grayish-pink growth, measuring 9 by 7 by 4 cm., that involved the anterior basal segment of the lower lobe, lingula and anterior segment of the upper lobe. Mediastinal nodes were not involved.

The patient recovered satisfactorily, and three weeks later was given a course of x-ray therapy. Her subsequent course was uneventful, and she has remained free of recurrence for six months.

Case 7—A 4-year-old boy was admitted to the hospital because of fever of unknown origin of 9 months' duration. One year prior to admission, he had developed a chronic otitis media with persistent purulent drainage. On admission the concentration of hemoglobin was 10.8 gm., the leukocyte count was 5000, and the sedimentation rate was 39 mm. in 1 hour. Roentgenographic examination revealed left pleural effusion. Repeated aspirations relieved episodes of dyspnea. Examination of the aspirated fluid for malignant cells was negative. Bronchoscopy also showed no abnormality. Subsequently, empyema developed, and open pleural drainage was advised.

At thoracotomy on January 12, 1959, the left lower lobe was adherent to the chest wall. No free pleural fluid was found. The entire lower lobe and part of the lingula of the left lung were airless, indurated, and fleshy. Due to the poor respiratory status,

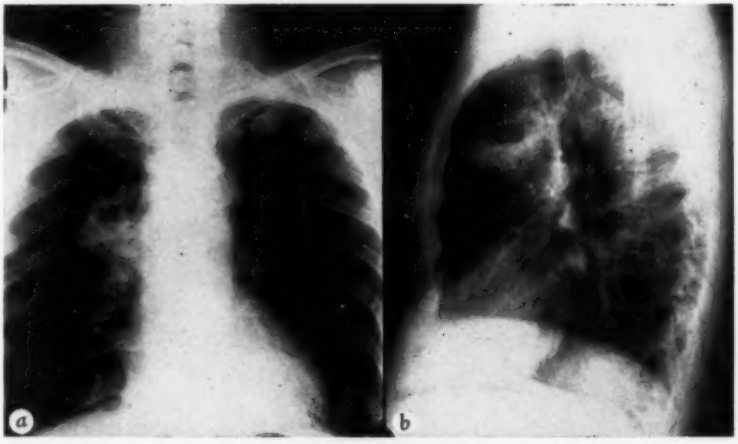

FIGURE 4 (Case 8): Malignant lymphoma, Hodgkin's granuloma type. *a*. A cavity is seen in the mass in the right upper lobe. The border of the lesion is sharply demarcated. *b*. The cavity is better illustrated in the lateral projection.

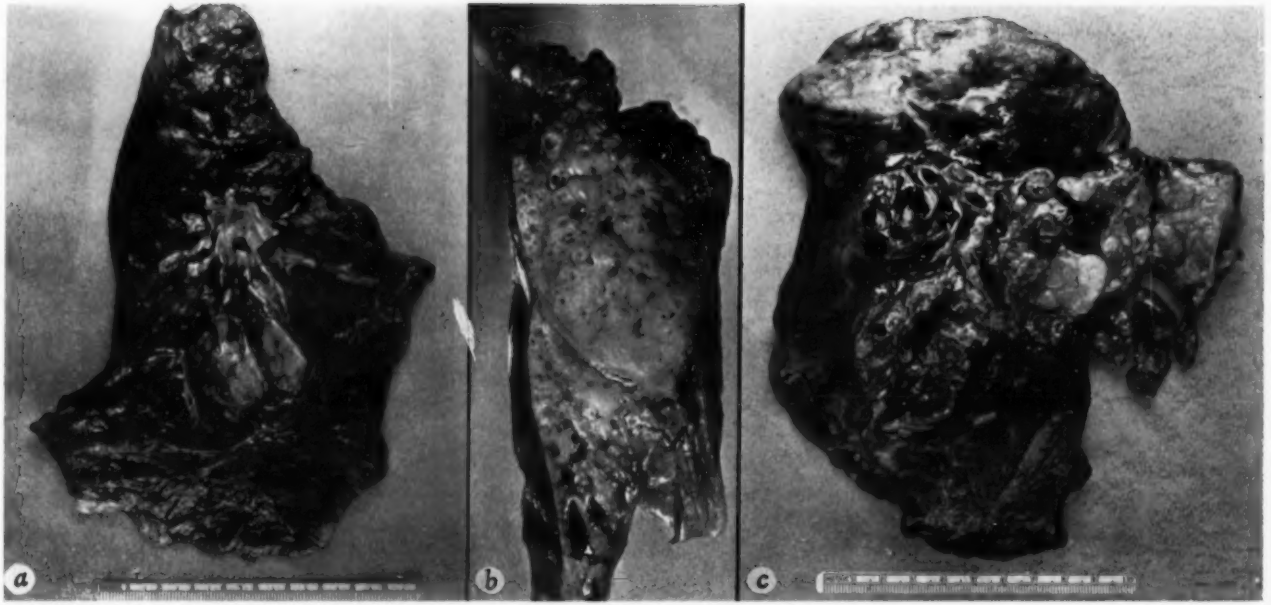

FIGURE 5: Surgical specimens. *a* (Case 1). Right lower lobe. A homogeneous, grayish-tan mass measuring 2 by 2.5 by 2 cm. is infiltrating the parenchyma near a segmental bronchus. Tumor is a malignant lymphoma, lymphocytic type. *b* (Case 5). Right middle and lower lobes. The cut surface of the tumor has a consolidated appearance with involvement of both lobes and the interlobar fissure. Evidence of obstructive pneumonitis with abscess formation should be noted. The tumor is a malignant lymphoma, lymphocytic type. *c* (Case 8). Medial surface of the right upper lobe, showing a well-circumscribed cavitating mass in the lower portion of the lobe. Hilar and mediastinal involvement should be noted. The tumor is a malignant lymphoma, Hodgkin's type.

pneumonectomy was deemed too risky a procedure, so left lower lobectomy was performed. On pathologic examination, the parenchyma of the left lower lobe was infiltrated by a malignant lymphoma of lymphoblastic type.

The child's postoperative course was complicated by high fever and persistent drainage from the chest, but he eventually recovered. Two weeks after operation, a course of roentgen therapy was given. Shortly thereafter, a bronchopleural fistula developed and the child died rather suddenly.

Case 8—A 49-year-old man registered at the clinic in September, 1957, because of hemoptysis and thoracic pain for the last 9 months. The concentration of hemoglobin was 12.4 gm., the leukocyte count was 8700, and the sedimentation rate was 48 mm. in one hour. On roentgenographic examination, a cavitating lesion was demonstrated in the right upper lobe (Fig. 4*a* and *b*). Bronchoscopy and cytologic studies of pulmonary secretions were not diagnostic.

Right thoracotomy was performed on September 21, 1957. A large tumor was found in the anterior segment of the upper lobe and extended into the middle lobe. Several large mediastinal nodes were present; biopsy of one of these disclosed Hodgkin's disease. Since the lesion was cavitary, removal seemed indicated, even though the process involved the deep mediastinal nodes. Accordingly, the right upper lobe and the right mediastinal, paratracheal, and subcarinal lymph nodes were removed. The nodular tumor mass in the right upper lobe contained a large cavity (Fig. 5*c*). Microscopically, the typical pathologic picture of Hodgkin's granuloma was seen (Fig. 6*b*).

After operation the patient received a course of x-ray therapy and did well for 1½ years. In March, 1959, an infiltrative process appeared in a thoracic roentgenogram. Nitrogen mustard therapy resulted in regression of the lesion.

Case 9—A 70-year-old retired engineer was admitted to the hospital with complaints of cough, fever, night sweats, and loss of ten pounds in ten weeks. The level of hemoglobin was 9.7 gm., leukocyte count was 5600, and sedimentation rate was 130 mm. in one hour. Roentgenographic examination demonstrated only atelectasis of the left upper lobe. On bronchoscopic examination extrinsic pressure was noted which narrowed the bronchus to the left upper lobe, although there was no apparent intraluminal mass. Studies of sputa and bronchial washings were repeatedly negative for malignant cells.

At exploratory thoracotomy on March 21, 1959, the left upper lobe of the lung was consolidated and there were many pleural adhesions. Examination in fresh frozen sections of one of the several enlarged hilar nodes disclosed Hodgkin's granuloma. Left pneumonectomy was performed. On pathologic examination, the upper lobe of the lung was infiltrated and its bronchus obstructed by a malignant lymphoma of Hodgkin's granuloma type, which measured 8 by 7 by 5 cm. An adjacent peribronchial node and two hilar lymph nodes were involved. The remainder of the lobe showed obstructive pneumonitis.

The patient did well initially, but on the second postoperative day congestive heart failure developed and death occurred in spite of intensive medical therapy.

Case 10—A 37-year-old farmer was first seen here in June, 1958, complaining of cough, fever, and hemoptysis of three weeks' duration. Thoracic roentgenograms revealed a mass at the right hilus (Fig. 3*b*), and subsequent bronchoscopic examination, an unusual blue, cystlike lesion at the opening of the right lower lobe bronchus immediately below the orifice of the medial basilar segment. This lesion was easily removed by bronchial biopsy, which suggested that it might be a blood clot. Biopsy was interpreted as showing an undifferentiated malignant neoplasm of large cell type. Hemograms were normal, but the sedimentation rate was 42 mm. in one hour. Studies of the sputum and bronchoscopic washings were negative for malignant cells. On June 27, 1958, right thoracotomy was performed. A large mass filled the hilus at the lower and middle lobes, although the upper lobe seemed entirely free of involvement. The tumor extended to the origin of the inferior pulmonary vein so that it was necessary to divide the vein at its atrial attachment. A large mass of nodes measuring 3 by 4 by 4 cm. lay behind the left atrium and were removed with the specimen. Additional nodes at the carina were removed and were not invaded.

On pathologic examination, there was a multinodular reticulum cell sarcoma 7 by 10 by 6 cm. near the hilus and involving the peribronchial tissue of both lobes. The growth had produced an associated obstructive pneumonitis and a portion of the

TABLE 3—COMPLAINTS WHEN FIRST SEEN BY PHYSICIAN, AND ROENTGENOGRAPHIC FINDINGS

Complaint	Patients	X-ray findings	Patients
Cough	9	Mass	10
Fever	8	Cavitation	4
Loss of weight	6	Atelectasis	5
Dyspnea	5	Pulmonary infiltration	2
Hemoptysis	5	Obstructive emphysema	1
Wheezing	4	Pleural effusion	1
Pain	2		
None	4		

right lower lobe showed extensive infarction. Multiple hilar nodes were involved by the tumor. On microscopic examination, abundant reticulin fibrils could be demonstrated between the malignant reticulum cells (Fig. 6c).

The patient made a satisfactory recovery from the operation and was given roentgen therapy. Four months later a follow-up roentgenogram of the thorax showed a lytic lesion in the right clavicle. Soon after this, the patient died from what his physician in his home locality believed to be pneumonia. Necropsy was not done.

Clinical Findings

These ten cases are summarized in Table 1 and the nine cases that formed the basis of the previous report by Cooley, McDonald and one of us (O. T. C.),[4] in Table 2. Examination of the combined data shows an essentially equal sex distribution of nine male and ten female patients. The average age at the onset of the disease was 43.5 years, with a range of 4 to 70 years. The average presurgical duration of symptoms in 11 cases of the lymphocytic or lymphoblastic type was 12 months. However, the average duration of symptoms in six cases of primary Hodgkin's disease of the lung was 3½ months. Three of the patients with malignant lymphoma of the lung had had symptoms for two or more years, and one had a lesion apparent on thoracic roentgenograms for 18 months before resection of the lesion was performed. In this case the surgeon felt that he had completely extirpated the disease by the pneumonectomy. The two patients with reticulum cell sarcoma had symptoms for one and two months before coming to operation.

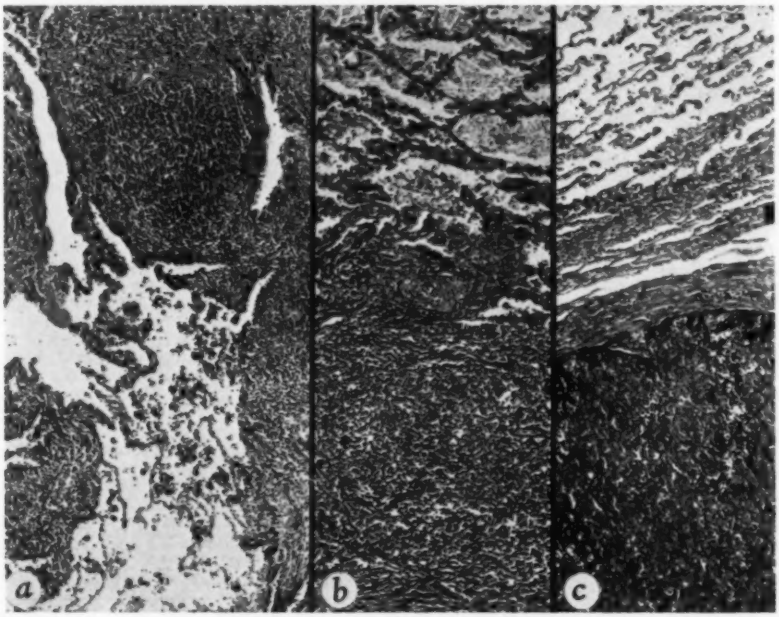

FIGURE 6: Malignant lymphomas in Cases 1, 8 and 10. *a* (Case 1). Periphery of lymphocytic type of tumor showing nodules of lymphoma cells, infiltrating alveolar septa and peribronchial connective tissue. Bronchiole surrounded by lymphoma, upper left (hematoxylin and eosin; x50). *b* (Case 8). Hodgkin's type. Section of the margin of the tumor which is relatively well-demarcated and has minimal involvement of adjacent alveolar septa (hematoxylin and eosin; x65). *c* (Case 10). Reticulum cell type. Section from the periphery of the tumor revealed a well-demarcated border with some compression of adjacent alveoli and minimal infiltration by lymphoma cells (hematoxylin and eosin; x60).

The type and incidence of symptoms that constituted the patient's complaint are itemized in Table 3. Cough present in nine cases and fever in eight were the most frequent symptoms. Dyspnea was present in five cases and the lesion was without pulmonary symptoms but was found first on routine examination of the thorax in four.

The only laboratory finding that was consistently abnormal was the sedimentation rate; it was significantly elevated in 14 of the 19 cases.

Roentgenographic and Bronchoscopic Findings

Roentgenographic findings, tabulated in Table 3, fall into the following categories: (1) the finding of a coin lesion in the lung (Fig. 1*a*), (2) obstructive emphysema as illustrated in inspiration-expiration roentgenograms (Fig. 2*a*), (3) a mass alone (Fig. 3*a* and *b*), (4) atelectasis with or without a demonstrable mass (Fig. 2*b*), (5) a diffuse infiltrative process (Fig. 1*b*), (6) the presence of a cavitating mass (Fig. 4*a*) and (7) pleural effusion. Cavitation occurred in six cases. Four of the cavities were recognized on roentgenograms, and the other two were seen when the tumor was examined. Four of the cavities occurred in Hodgkin's disease, and the other two in malignant lymphoma of the lymphocytic type. A third of the patients showed roentgenographic evidence of bronchial obstruction, either on the basis of atelectasis in five patients or obstructive emphysema in one patient.

In 10 of the 17 cases in which bronchoscopy was done, the lesion was found to contribute to the narrowing of the involved bronchus (Table 4). In four cases the tumor was seen by bronchoscopy, and a positive biopsy obtained. Pulmonary cytologic studies for malignant cells in 16 cases were considered negative.

Pathologic Features

The extent of the lesions seen in the 19 cases encountered at the Mayo Clinic is summarized in Table 5. In 11 cases the malignant lymphoma was lymphocytic; in two of these the lesions were predominantly immature lymphocytic (lymphoblastic) type. In six cases the diagnosis was Hodgkin's disease, and in two cases, reticulum cell sarcoma. A follicular component as noted by Sternberg and associates[10] was found in three of seven cases of lymphocytic lymphoma in the present series.

The patients with either Hodgkin's disease or reticulum cell sarcoma consistently had more advanced disease at the time of surgical exploration than the patients with malignant lymphoma of the mature or immature lymphocytic type. In four (37 per cent) of the 11 cases of lymphocytic lymphoma, the hilar nodes were involved; the mediastinum apparently was not involved in any case. In five (83 per cent) of the six cases of Hodgkin's disease, the hilar nodes were involved, and in four

TABLE 4—RESULTS OF BRONCHOSCOPIC EXAMINATION AND OF BRONCHIAL WASHINGS IN 19 PATIENTS

	Result		Test
	Positive	Negative	not done
Aberration of bronchi	10	6	3
Pulmonary cytology for malignant cells	0	16	3

(67 per cent) mediastinal nodes were involved. In both cases of reticulum cell sarcoma hilar and mediastinal nodes were involved. Thus involvement of the hilar lymph nodes was found in 11 (58 per cent) and involvement of the mediastinal nodes in six (32 per cent) of the 19 cases of primary malignant lymphoma of the lung.

The various types of malignant lymphoma exhibited certain gross differences. In three of the 11 cases of lymphoma of the lymphocytic type, the tumor was lobar in distribution so that usually the entire lobe and even adjacent segments were involved by the invasion of lymphoma cells. Also bilateral pulmonary involvement by lymphocytic lymphoma was proved in Case 3 at necropsy and was suggested in the roentgenologic

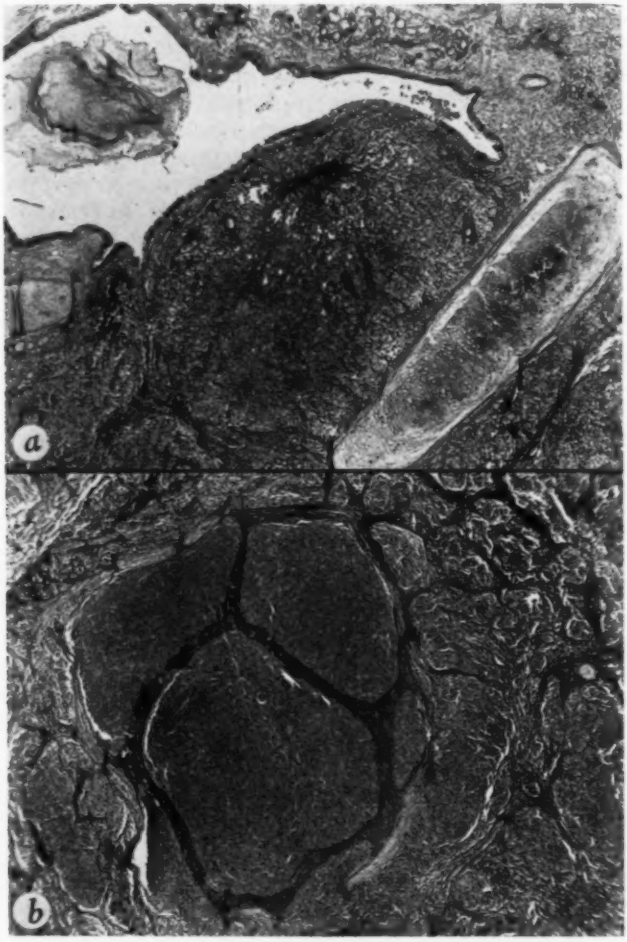

FIGURE 7: Malignant lymphomas, lymphocytic type, of the lung in Cases 2 and 3. *a* (Case 2). Cross section of a bronchus which is narrowed by submucosal lymphomatous infiltration; however, the epithelium is intact (hematoxylin and eosin; x20). *b* (Case 3). The prominent follicular component shown here was surrounded by a homogeneous field of lymphocytes (hematoxylin and eosin; x24).

findings in Case 4. At the time of operation the involved lung was often described as being heavy, indurated and of fleshy consistency, and on pathologic examination the cut surface of the tumor was homogeneously gray or grayish tan. In the other eight cases of lymphocytic type the lesion presented as a more localized mass that incompletely involved a lobe but was not sharply circumscribed in its periphery. In the Hodgkin's and reticulum cell types of lymphoma, the lesion was a more sharply circumscribed or nodular mass which involved larger bronchi and was partially necrotic and gray to yellowish gray in color. These lesions at times grossly resembled a bronchogenic carcinoma. The impression of a more circumscribed periphery for these latter tumors than for the lymphocytic lymphomas was borne out in examination of the microscopic sections. In the lymphocytic type of lymphoma, as indicated by Sternberg and associates,[10] the advancing periphery of the neoplasm within the parenchyma of the lung was made up of nodules of lymphoma cells which could be seen infiltrating pulmonary septa and peribronchial connective tissue beyond the gross apparent margin of the tumor. In the Hodgkin's and reticulum cell types the microscopic periphery of the neoplasms in the lung was more sharply demarcated, and the tumor apparently advanced in a more compact mass without peripheral nodularity. Roentgenographically, the lymphocytic type had a more feathery peripheral margin when compared to the other types, which correlates well with the histologic findings (Fig. 3*a*).

In eight of the 11 cases of lymphocytic type of malignant lymphoma that presented as localized masses, in addition to the four cases of resection for Hodgkin's disease and the one case of resection for reticulum cell sarcoma, the lymphoma cells could be seen to encroach on the lumen of bronchi or bronchioles by bulging out from the submucosa, although the overlying respiratory epithelium was usually intact (Fig. 7*a*). Peribronchial and submucosal infiltration may produce concomitant atelectasis or obstructive pneumonitis or both.

Prognosis

From the questionnaire recently returned by the survivors the data on survival in Tables 1 and 2 have been compiled. There were five hospital deaths, a mortality rate of 26 per cent. Four other deaths occurred from 4 to 42 months after operation. One patient, whose lesion was considered too extensive to be removed surgically, was lost to follow-up. Two patients are alive with known recurrences. Seven patients are living and well. Of the nine patients operated on 5 or more years ago, two are well and

TABLE 5—EXTENT OF LESION IN 19 CASES

One lung	9
One lobe*	5
Two lobes	2
Inoperable	3
One was bilateral†	

*Case 4 also had an indeterminate infiltrate in the opposite lung which cleared following roentgen therapy.

†Case 3 had histologically proved lymphocytic lymphoma in the opposite lung at necropsy.

one is living with a known recurrence, for a five-year survival rate of 33 per cent, and one has been lost to follow-up. Of the ten who have been operated on subsequent to 1954, two have survived two or more years, and four others are living and well, having had their operation less than two years ago.

Comment

Primary lymphoma of the lung is usually considered an indolent disease that should respond well to excision of the lesion.[10] It also has been suggested that this assumption is not valid for primary Hodgkin's disease of the lung and that this disease carries with it a more serious prognosis. Although the duration of symptoms before discovery was shorter in Hodgkin's disease and reticulum cell sarcoma than in the lymphocytic type of lymphoma, still the Hodgkin's lymphomas and reticulum cell sarcomas in our series were uniformly more advanced by the time thoracotomy was performed—as indicated by the fact that surgical treatment was not possible for three lesions, pneumonectomy was required for three others and two lobes were removed for two others. Follow-up studies do not show any long-term, recurrence-free survivors in the group with Hodgkin's disease or reticulum cell sarcoma.

The incidence of dyspnea was somewhat surprising, and in this series it occurred only in the lymphocytic type of lymphoma. Anatomically one might suggest that the more prominent alveolar septal infiltration or lobar distribution might account for this finding. Of interest is the report of a case of a diffusion type of defect found in pulmonary function studies of a patient with a lymphocytic type of pulmonary lymphoma.[19]

Since primary lymphoma of the lung does not begin as an intraluminal mass, it might be supposed that bronchoscopic examination would yield little or no information. Notable then are the ten cases in which aberrations of the bronchial tree were found on bronchoscopy. Four of these patients had positive bronchoscopic biopsies. Numerous reports in the literature suggest that a positive biopsy might be obtained in cases of primary Hodgkin's disease of the lung.[4,5,15-17] Further evidence that the bronchus might be encroached on by the lesion is the fact that about a third of the patients showed roentgenologic evidence of bronchial obstruction, either in the form of distal atelectasis or obstructive pneumonitis and in one case by obstructive emphysema.

A variety of roentgenographic patterns are produced by primary malignant lymphoma of the lung. There is no typical roentgenographic manifestation of this disease. However, it is of interest that cavitation could be identied from roentgenograms in four cases; three of these were of Hodgkin's type and one of lymphocytic type of pulmonary lymphoma. This finding has been reported previously in the literature.[4,16,20-22] Also of interest is the fact that the lymphocytic type of lymphoma presented either roentgenographically or at gross pathologic examination or at both as a diffuse lobar process or as a localized infiltrative process in the lung.

The histologic similarity of these lesions to small cell carcinomas in the lung[23] and in the stomach as well[24] is illustrated in the four cases in this series in which bronchoscopic biopsy was positive. In three of the four cases the differential diagnosis of malignant lymphoma from undifferentiated carcinoma of the small cell type was difficult, and the final decision required obtaining additional tissue for microscopic examination.

The observation expressed by Stout[24] that two different biologic types of lymphoma based on the rapidity of their progression exist finds support in the fact that in all of the patients who had lesions that were suspected of being present for a long period, based on the duration of symptoms, resection with a chance for cure was possible, and such patients are the ones who have survived in our series. One of these patients, who had symptoms 36 months prior to operation, has survived for 13 years after removal of the lesion. The prognosis for malignant lymphoma situated in the lung, however, is apparently not as favorable as that for primary lymphomas in the stomach.

Most of our patients received roentgen therapy in combination with the surgical treatment. The suggestion that it is a valuable adjunct to surgical therapy is made by the fact that in four cases objective remission was seen to occur after a therapeutic course. This agrees with reported favorable results after roentgen therapy.[14,16,17,25] Roentgen therapy following pulmonary resection too closely may be injudicious, because unless three to four weeks are allowed to pass after operation the bronchial stump may not heal well, and a bronchopleural fistula may result.

SUMMARY

The clinical and pathologic features of ten patients treated surgically for primary pulmonary lymphoma and a follow-up comparative study of nine cases previously reported are presented.

The most common symptoms were cough and fever of variable duration, although about 25 per cent of the patients were asymptomatic. No roentgenographic manifesta-

tions could be considered typical of this disease, although in 16 of the 19 patients thoracic roentgenograms suggested a neoplastic process. Cavitation was seen in six of the entire group including two thirds of the patients with Hodgkin's disease.

Significant bronchoscopic findings were noted in ten of the 19 cases, and in four, biopsy was positive.

Pulmonary, hilar and mediastinal involvement was usually more extensive in Hodgkin's disease and reticulum cell sarcoma than in malignant lymphoma of the lymphocytic or lymphoblastic type, although the duration of symptoms before the patient consulted a physician was longer in the last group.

Nine of 19 patients are still living, seven without clinical or roentgenologic evidence of lymphoma; two of these seven have survived five or more years.

The present study indicates that primary pulmonary malignant lymphomas of the lymphocytic type behave more favorably than Hodgkin's granuloma or reticulum cell sarcoma. The treatment suggested for primary pulmonary lymphoma is surgical excision which may be supplemented by irradiation therapy if the intrathoracic disease is extensive.

RESUMEN

Se presentan las características clínicas y patológicas de diez enfermos de linfoma primario pulmonar, tratados quirúrgicamente y el seguimiento, para fines comparativos, de nueve casos antes presentados. El síntoma mas común fué la tos y la fiebre de duración variable aunque aproximadamente el 25 por ciento de los enfermos fueron asintomáticos. No hubo manifestaciones radiográficas que pudieran considerarse como típicas de la enfermedad, aunque en 16 de 19 enfermos los roentgenograms del tórax sugirieron una enfermedad neoplásica. Se observó excavación en seis del grupo incluyendo dos tercios con enfermedad de Hodgkin.

Hubo hallazgos significantes a la broncoscopía en 10 de los 19 y en 4 la biopsia fué positiva.

El compromiso pulmonar, hiliar y mediastinal, fué habitualmente mas extenso en la enfermedad de Hodgkin y en sarcoma reticulo-celular que en el linfoma maligno de los tipos linfocítico o linfoblástico, aunque la duración de los síntomas antes de que el enfermo consultase al médico fué mas larga en el último grupo.

Nueve de los 19 enfermos aún viven, siete sin evidencia clínica o radiológica de linfoma dos de esos siete han sobrevivido por 5 o mas años.

Este estudio indica que los linfomas pulmonares primarios malignos del tipo lifocítico se conducen mas favorablemente que el granuloma de Hodgkin o el sarcoma reticulocelular. El tratamiento sugerido para el linfoma primario pulmonar es la excisión quirúrgica que puede completarse con radiación si la enfermedad intratorácica es extensa.

RESUMÉ

L'auteur présente les caractéristiques cliniques et pathologiques de 10 malades traités chirurgicalement pour adénopathie médiastinale maligne primitive et une étude comparative de 9 cas précédemment rapportés.

Les symptômes les plus communs furent la toux et la fièvre, de durée variable, bien qu'environ 25% des malades aient été asymptomatiques. Aucune manifestation radiologique ne put être considérée comme typique de cette affection, bien que 16 des 19 malades eussent des radiographies évoquant un processus néoplastique. Des cavernes furent notées chez 6 malades du groupe, comprenant deux tiers des malades atteints de maladie de Hodgkin.

Des constatations bronchoscopiques significatives furent notées dans 10 des 19 cas, et chez quatre la biopsie fut positive.

L'atteinte pulmonaire, hilaire et médiastinale fut habituellement plus extensive dans la maladie de Hodgkin et le réticulo-sarcome que dans le lymphome malin de type lymphocytique ou lymphoblastique, bien que la durée des symptômes avant que le malade ne vienne consulter fut plus longue dans le dernier groupe.

Neuf des 19 malades sont encore en vie, sept sans preuve clinique ou radiologique de lymphome; deux de ces sept malades ont survécu 5 ans ou plus.

La présente étude montre que les lymphomes pulmonaires primaires malins de type lymphocytique se comportent plus favorablement que la maladie de Hodgkin et que le réticulosarcome. Le traitement suggéré pour le lymphome pulmonaire primaire est l'exérèse chirurgicale, qui peut être complétée par irradiation si la maladie intrathoracique est extensive.

ZUSAMMENFASSUNG

Es wird ein Bericht vorgelegt über die klinischen und pathologischen Befunde von 10 wegen primärem pulmonalem Lymphom chirurgisch behandelten Kranken, sowie eine vergleichende Nachuntersuchung von 9 bereits früher mitgeteilten Fällen.

Die häufigsten Symptome bestanden in Husten und Fieber von verschiedener Dauer, obwohl etwa 25% der Patienten symptomfrei waren. Keine röntgenologischen Manifestationen konnten als typisch für diese Erkrankung bezeichnet werden, obwohl bei 16 von den 19 Kranken die Thorax-Röntgenaufnahme einen neoplastischen Prozess vermuten liessen. Cavernenbildung ergab sich in 6 Fällen aus der gesamten Gruppe einschliesslich zwei Drittel der Patienten mit Hodgkin'scher Krankheit.

Signifikante bronchoskopische Befunde wurden bei 10 der 19 Fälle festgestellt, und bei 4 verlief die Biopsie positiv.

Die pulmonale, hiläre und mediastinale Beteiligung war gewöhnlich stärker ausgeprägt bei Hodgkin'scher Erkrankung und bei Retikulum-Zellsarkom als beim malignen Lymphom von lymphocytären oder lymphoblastischen Typ, obwohl die Dauer der Symptome vor Konsultation eines Arztes durch den Kranken länger war in der letzten Gruppe.

Neun der 19 Patienten sind noch am Leben, sieben ohne klinische oder röntgenologische Anhaltspunkte für ein Lymphom; zwei von diesen sieben lebten bereits 5 Jahre oder länger.

Die vorliegende Untersuchung zeigt, daß primäre pulmonale bösartige Lymphome vom lymphocytären Typ sich günstiger verhalten als Hodgkins'sche Granulome oder Retikulum-Zell-Sarkome. Die für das primäre pulmonale Lymphom vorgeschlagene Behandlung besteht in der chirurgischen Exzision, die durch Strahlentherapie ergänzt werden kann, falls ein ausgedehnter intrathorakaler Prozess vorliegt.

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Inhalation of Varying Concentrations of Oxygen in the Treatment of Severe Pulmonary Insufficiency*

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Acute pulmonary insufficiency in chronic pulmonary disease is a medical emergency. Its therapy is difficult, and the mortality is great. A number of approaches to the problem have been employed, including the use of antibiotics, corticosteroids, oxygen, tracheotomy, and various mechanical devices to improve respiration. The physiologic derangement seen in this condition is relatively constant although it may occur in a wide variety of diseases. There is severe arterial hypoxia and hypercapnia. Associated with the persistent hypercapnia is a decreased sensitivity of the respiratory center to the stimulus of carbon dioxide. The sole remaining stimulus to respiration is the hypoxia. When the arterial oxygen is increased above physiologic levels, such as occurs during breathing of 100 per cent oxygen, this stimulus is lost, alveolar ventilation decreases, arterial hypercapnia increases, the pH of the arterial blood decreases, and death ensues.

In order to decrease the hypercapnia or minimize its increase and, at the same time, prevent severe hypoxia, oxygen in concentrations of *less than* 100 per cent was used in the treatment of this condition. The sensitivity of the medullary respiratory center to P_{CO_2} may thus be gradually increased. What role the increased arterial oxygen plays in this improvement is unknown.[1] The observations obtained from this form of therapy are the subject of this report.

Methods

All patients evaluated had chronic pulmonary disease, but of different etiologies. They were acutely ill with severe pulmonary insufficiency at the time of these observations.

Studies were performed with the patients breathing ambient air, 100 per cent of oxygen by nasal catheter, and varying concentrations of oxygen administered by IPPB/I (intermittent positive pressure breathing, inspiratory). Arterial blood samples were obtained and analyzed for oxygen and carbon dioxide tensions by the Riley bubble technique.[2] Admittedly, this is not the most accurate procedure available, but with a well-trained biochemist, periodically checked by tonometer studies, the physician at the bedside can quickly obtain valuable clinical information which will give an objective approach to further treatment. Varying concentrations of inspired oxygen were obtained by mixing compressed air and 100 per cent oxygen in the nebulizer of a Bennett Model PR-1A Respirator.

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Results

Table 1 illustrates the role of varying the concentrations of oxygen in the treatment of these emergency problems. Some of the data presented concern the early cases for which equipment was not yet available to deliver the necessary low-oxygen concentrations. These patients (Table 1, cases R.M.W., A.T.F., and G.C.) did not do well physiologically although some of them did improve clinically.

One of us (D.D.) then improvised a method of mixing compressed air with 100 per cent oxygen in the IPPB/I apparatus† in order to secure the desired concentrations of oxygen for inhalation. The most effective levels of inspired oxygen in these patients were found to lie between 25 and 35 per cent with 12 centimeters of water pressure. The physiologic improvement in these cases, as shown by arterial oxygen and carbon dioxide tensions, was paralleled by clinical improvement. As may be seen in the case of A.F., the breathing of either mixture under pressure relieved the hypoxemia, but the breathing of 32 per cent O_2 was associated with a higher arterial CO_2 tension than was the breathing of 27 per cent O_2. In view of the effects of respiratory acidosis and the increased prospect of narcosis and coma as a complication of arterial hypercapnia, one should choose the inspired oxygen concentration which raises the arterial O_2 tension within physiological limits. This must be done, however, without increasing the hypercapnia and possibly decreasing it. Clinically, in these

TABLE 1—ARTERIAL GAS TENSIONS BEFORE AND AFTER OXYGEN THERAPY

Patient	Before Trial Therapy P_{O_2}*	Before Trial Therapy P_{CO_2}*	Method of Oxygen Administration Per cent Oxygen (Approximate)		After Trial Therapy P_{O_2}*	After Trial Therapy P_{CO_2}*
R.M.W.	39	62	40	IPPB/I 20 minutes, 12 cm.H_2O	118	76
A.T.F.	26	77	40	IPPB/I 12 minutes, 12 cm.H_2O	108	93
G.C.	68	83	40	IPPB/I 15 minutes, 12 cm.H_2O	252	97
J. A.	22	73	40	IPPB/I 15 minutes, 18 cm. H_2O	64	100
			73	IPPB/I 15 minutes, 12 cm.H_2O	76	90
			100	Nasal catheter 1 hour, 8 liters per minute	49	80
M.K.	27	59	35	IPPB/I 15 minutes, 12 cm.H_2O	150	64
			27	IPPB/I 15 minutes, 12 cm.H_2O	116	69
			100	Nasal catheter 15 minutes, 5 liters per minute	87	63
R.W.	51	74	21	IPPB/I 10 minutes, 12 cm.H_2O	45	80
			30	IPPB/I 10 minutes, 12 cm.H_2O	100	67
A.F.	32	77	32	IPPB/I 15 minutes, 12 cm.H_2O	154	74
			27	IPPB/I 15 minutes, 12 cm.H_2O	140	62

*Arterial oxygen and carbon dioxide tensions in millimeters of mercury.

†Manufactured by Bennett Respiration Products, Inc.

patients there seems to be an increase in tidal volume and a decrease in the work performed during respiration when IPPB/I is initiated.

It is interesting to note that in the case of M.K., despite the arterial oxygen tension 27 mm. Hg., the arterial carbon dioxide tension was only 59 mm. Hg. while breathing ambient air. This case, in contrast to case J.A., reveals how a relatively small increment in inspiratory O_2 concentration under pressure increased the arterial oxygen tension above the normal physiological limits. As will be brought out later, the patient's response to a given inspired oxygen concentration is dependent on his underlying respiratory defect.

Discussion

It should be emphasized that all of these patients were acutely ill, and oxygen therapy was therefore supplemented by other means of improving alveolar ventilation such as the employment of bronchorelaxants, antibiotics, corticosteroids, expectorants, etc. It is not the purpose of this paper to review or evaluate the numerous therapeutic agents or procedures that are utilized in the treatment of severe pulmonary insufficiency, but to demonstrate and discuss the physiologic basis for the use of oxygen.

Our studies tend to confirm the documented observation that relief of arterial hypoxemia with physiologic levels of arterial oxygen has little effect on minute ventilation in patients with pulmonary emphysema and carbon dioxide retention.[3] However, a considerable increase in arterial P_{O_2} such as occurs with breathing 100 per cent oxygen, elicits a marked decrease in minute ventilation.[3,4] This suggests that it is important to distinguish between physiologic and pathophysiologic levels of oxygen tension in the arterial blood.

We have also shown that it is not necessary to leave a patient severely hypoxic because of fear of apnea or alveolar hypoventilation. Because of economic reasons, we have chosen to vary the inspired oxygen concentration by diluting 100 per cent oxygen with compressed air (there is clinical evidence that helium-oxygen mixtures are effective in acute pulmonary insufficiency, but the expense involved precludes their routine use).[5]

The increase in arterial oxygen tensions to a given inspired concentration of oxygen will depend on the underlying pulmonary structural pathology present; consequently, no two patients will respond exactly alike. This is important physiologically because it emphasized the necessity of varying the concentration of inspired oxygen and of subsequently obtaining arterial samples in order to reach the point, in each patient, at which the arterial oxygen is within the physiologic range and the carbon dioxide has minimally increased or has decreased. Of course, the response to a given inspired oxygen concentration may change as is occasionally suggested by lack of clinical improvement. In such situation it will be necessary to repeat the arterial puncture in 12 to 24 hours.

Usually, our patients were withdrawn from IPPB/I in 36 to 96 hours. This depended on the reversibility of the acute stress on the limited pulmonary reserve and on the complications secondary to hypoxia. Patients have not only shown a change in the level of consciousness after treatment, but also changes in personality.

The effects of pressure breathing on ventilation and circulation have been reported by many investigators.[6-8] Numerous mechanical devices have been used in a variety of ventilatory disorders. The positive pressure applied to the patients with chronic pulmonary insufficiency during IPPB/I inflates the lung to a greater extent than during normal inspiration, thereby providing better alveolar ventilation and a more uniform distribution. However, it should be stressed that this therapy may produce unwanted changes in cardiopulmonary dynamics.[9] It should also be pointed out that without controlled respiration (such as with the use of succinylcholine) the use of respiratory body chambers (Emerson and Drinker types) in patients with obstructive pulmonary emphysema may further decrease the arterial P_{O_2} and increase the arterial P_{CO_2}. This is probably due to the increased work of breathing and the associated alveolar hypoventilation caused when the patient "fights" the respirator.

We have used the nasal catheter humidification technique employing different oxygen flows to obtain the arterial oxygen tension desired. However, this method has not always been physiologically or clinically successful. We have seen tachypneic patients respond to IPPB/I whose arterial oxygen tensions were not in the physiologic range on high oxygen flows through a nasal catheter. The danger of low oxygen flows (1 to 2 liters per minute) through a nasal catheter in patients with acute pulmonary insufficiency[10] is the persistence of severe hypoxia. This state may go unrecognized if arterial gas tensions are not determined.

SUMMARY

1. The management of the hypoxia of acute pulmonary insufficiency in chronic lung disease is often a difficult emergency problem.

2. Ideally, oxygen should be administered in this condition in such a way as to increase the arterial oxygen tension without aggravating the hypercapnia.

3. The choice of oxygen therapy will therefore depend on the response of the patient's arterial gas tensions to a given inspired oxygen concentration however delivered. This response will vary from patient to patient according to the pulmonary structural pathology present.

4. The importance of determining arterial gas tensions initially and after each variation in oxygen therapy is stressed. Repeated determinations in 12 to 24 hours may be indicated if clinical improvement does not occur.

5. Oxygen administered by the nasal catheter humidification technique may not be adequate. Low oxygen flows given by this method may actually prolong the hypoxic state.

6. A method is described in which varying oxygen concentrations were effectively employed in the IPPB/I (intermittent positive pressure, inspiratory) apparatus.

ADDENDUM: Since this article was submitted for publication, one of the authors (D.D.) has worked with Bennett Respiration Products, Inc. to produce a simplified and more physiologic method of delivering varying concentrations of inspired oxygen between 20 and 40 per cent. We have also incorporated into the machine nebulization on inspiration only. Below is a brief description of the apparatus that we have been using.

A Bennett pedestal IPPB Therapy Unit (Model PV-3P), with the air diluter modified to give approximately 35 per cent oxygen concentration when 100 per cent oxygen is used as the source gas. It is equipped with continuous and intermittent nebulizer needle valves, and served by two Puritan regulators with nebulizer needle valves and pressure compensated flowmeters, one calibrated for oxygen, the other for air, manifolded to a single outlet.

RESUMEN

1. El manejo de la hipoxia en la insuficiencia pulmonar aguda en la enfermedad pulmonar crónica es a menudo una emergencia difícil de resolver.

2. Idealmente el oxígeno debe ser administrado en estas condiciones de tal manera que aumente la tensión arterial del oxígeno sin agravar la hipercapnia.

3. La elección de la oxigenoterapia dependerá por tanto de la respuesta de las tensiones de gas arterial en los enfermos a una concentración dada de oxígeno. Esta respuesta será diferente de un enfermo a otro de acuerdo con la estructura patológica presente.

4. La importancia de determinar las tensiones de gas arterial inicialmente y después de cada variación en el tratamiento con oxígeno se hace resaltar. Las determinaciones repetidas en 12 a 24 horas pueden indicar si la mejoría clínica no ocurre.

5. La administración de oxígeno por el cateter nasal con humidifación puede no ser adecuada. El flujo del oxígeno dado por esta técnica puede de hecho prolongar el estado hipóxico.

6. Se describe un método en el que se emplearon concentraciones variantes de oxígeno con resultados efectivos con el aparato de presión intermitente positiva inspiratoria (IPPB/I).

RESUMÉ

1. La conduite thérapeutique de l'hypoxémie de l'insuffisance pulmonaire aiguë dans les maladies pulmonaires chroniques est souvent un problème d'urgence difficile.

2. Idéalement, l'oxygène devrait être administré dans cet état de telle sorte qu'on obtienne l'augmentation de la teneur oxygénée artérielle sans aggraver l'hypercapnée.

3. Le choix de la thérapeutique oxygénée dépendra alors de l'importance de la tension des gaz artériels du malade à une concentration donnée de l'oxygène inspiré. Cette réponse variera d'un malade à l'autre selon l'état pathologique de ses poumons.

4. L'auteur met l'accent sur l'importance qu'il y a à déterminer les tensions des gaz artériels au début et après chaque modification de la thérapeutique oxygénée. Des examens répétés toutes les douze ou 24 heures peuvent être nécessaires si l'amélioration clinique ne survient pas.

5. L'oxygène administré par la méthode d'humidification du cathéter nasal peut ne pas être convenable. Des taux faibles d'oxygène administrés par cette méthode peuvent prolonger l'état hypoxique.

6. L'auteur décrit une méthode dans laquelle des concentrations diverses d'oxygène sont effectivement utilisées dans un appareil à pression positive intermittente, inspiratoire.

ZUSAMMENFASSUNG

1. Die Behandlung der Hypoxie bei der akuten pulmonalen Insuffizienz während chronischer Lungenerkrankung ist oft ein schwieriges Problem akuter Dringlichkeit.

2. Im Idealfall sollte man Sauerstoff in einem solchen Zustand in der Weise geben, daß die arterielle Sauerstoff-spannung ansteigt, ohne daß der Kohlensäuregehalt des Blutes übermässig zunimmt.

3. Die Wahl der Sauerstofftherapie wird daher abhängig von der Reaktion der arteriellen Atemgasspannungen des Kranken bei einer trotzdem gegebenen und inhalierten Sauerstoffkonzentration. Diese Reaktion wird von Fall zu Fall verschieden sein entsprechend der vorliegenden pulmonalen Strukturveränderung.

4. Es wird die Wichtigkeit der Bestimmung der arteriellen Gasspannungen zu Anfang und nach jeder Veränderung der Sauerstofftherapie hervorgehoben. Wiederholte Bestimmungen innerhalb von 12 bis 24 Stunden können indiziert sein, wenn es zu keiner klinischen Besserung kommt.

5. Sauerstoffzufuhr in Form des Nasenkatheters mit Feuchtigkeitsregulierung ist nicht immer adäquat. Der niedrige mit dieser Methode gegebene Sauerstoffgehalt kann tatsächlich den hypoxischen Status noch verlängern.

6. Es wird eine Methode beschrieben, bei der verschiedene Sauerstoffkonzentrationen in dem Gerät für intermittierende positive Druckatmung in wirksamer Wiese zur Anwendung gelangte.

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ELECTROCARDIOGRAPHIC CHANGES IN DOGS DUE TO HYPOXIA

Changes in the electrocardiographic pattern induced by experimental hypoxia (7 per cent in O_2 in N_2) in a group of 13 dogs are described. During hypoxia, in most of the dogs, an increase to the positive potential of the T wave and of the Q-T time has been observed. These findings would indicate that hypoxia causes, in the dog, a lengthening of the "activation" time of the subendocardial layers of the myocardium, in contrast with the phenomena that take place under comparable conditions in normal human subjects and in patients with coronary disease.

Bergamasco, G. L., Binda, G. and Soldati, B.: "Il comportamento dell'elettrocardiogramma del cane normale in ipossia," *Atti, Accad. Med. Lombarda*, 15:315, 1960.

Colloquium on New Antituberculosis Drugs*

Criteria for Assaying New Antituberculosis Drugs, Evaluation of Kanamycin, D-Cycloserine and α Ethylthioisonicotinamide in the Therapy of Pulmonary Tuberculosis

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Considerable progress has been made during the last few years in the fight against tuberculosis. Intelligently combined application of various measures—vaccination with BCG, early detection and elimination of the sources of infection by systematic examination of the population and of the people in the environment of new cases, chemoprophylaxis, immediate and sufficiently long-lasting treatment with antituberculosis drugs, timely surgical intervention and public health measures—can lead to the eradication of tuberculosis. Many countries still have a long way to go toward the realization of this aim.

As far as treatment of tuberculosis with specific medicaments is concerned, we have today only one antituberculosis drug at our disposal which, in tolerance and efficacy, meets to a certain extent our theoretical and practical requirements, namely: isoniazid. All other active substances so far used in therapy of tuberculosis show more or less pronounced shortcomings either in tolerance or in efficacy or in both.

In order to obtain real progress in the chemotherapy of tuberculosis, we urgently need at least two other preparations which equal or surpass isoniazid in tolerance and efficacy and which, in addition, possess a different mechanism of action. It was appropriate, therefore, that this up-to-date subject should be discussed during the Sixth International Congress on Diseases of the Chest. The discussion took the form of a Colloquium at which renowned specialists from many countries under the chairmanship of Professor B. Fust (Basle) and Professor E. Bernard (Paris), laid down generally recognized criteria for the experimental and clinical examination of new antituberculosis drugs, and afterward, tried to assess the present status of a few more recent preparations in the therapy of pulmonary tuberculosis.

About 130 persons participated in the Colloquium, of whom about one fourth took an active part in the discussions. Apart from the introductions of the two chairmen, statements read by E. Freerksen (Borstel, Germany), J. Hein (Tönsheide, Germany), A. O. Zorini and G. Spina (Italy), G. F. von Krogh (Falkenstein, Germany), E. A. Piszczek (Forest Park, Illinois, U.S.A.), J. Regli (Heiligenschwendi, Switzerland) and G. Berg (Borstel, Germany) contributed greatly to the clarification of still unsettled questions. The lively discussion, which was considerably facilitated by skilled translation, showed how great was the general interest in these problems.

This report endeavors to summarize the most important results of the Colloquium.

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*Presented at the Sixth International Congress on Diseases of the Chest, American College of Chest Physicians, Vienna, Austria, August 28-September 1, 1960.

I. Criteria for the selection of antituberculosis drugs in the experiment

The propositions made by Fust in his introduction of this item of the program were unanimously accepted. Accordingly, isoniazid is recommended as "standard" preparation and only substances which equal or surpass isoniazid in tolerance and efficacy and which, in addition, possess a different mechanism of action, can be considered to represent a real advance. Tolerance, as well as antituberculosis action of such substances, have to be tested *in vivo*, using as large a variety of animal species and modes of infection for the evaluation as possible. A mechanism of action differing from that of isoniazid can easily be recognized in the *in vivo* experiment with tubercle bacilli of the human type which are highly resistant to isoniazid.

The participants further accepted the proposition of the chairman, that isoniazid be taken also as clinical "standard" for new antituberculosis agents. There was, furthermore, agreement with his opinion that such preparations which are markedly inferior to isoniazid in respect of tolerance or activity or both, or which do not possess a different mechanism of action, signify no progress and therefore do not deserve to be tested clinically. Until preparations can be found which meet the established criteria, clinical use must be made of those of lesser quality which are on the market.

II. Criteria for clinical examination and evaluation of newer antituberculosis drugs

It is generally accepted that tolerance, as well as antituberculosis action can only be adequately demonstrated when the medicament to be tested is used alone.

a) *Tolerance* of the new substance is best tested in patients with chronic pulmonary tuberculosis who have previously been given all other specific drugs known to be effective, without lasting benefit. In such patients, the tolerance test is also justified because they might profit from the antituberculosis effect of the new medicament. Apart from careful clinical observation, regular and frequent blood counts, kidney and liver function tests, including determination of residual nitrogen, are necessary. These tolerance studies should be continued for at least three months.

b) Clinical testing of the *antituberculosis activity* of a preparation is justified only when the incidence and degree of side effects are less than, or not markedly in excess of those observed with isoniazid.

   1) For *clinical trials, patients* should be chosen with active, open pulmonary tuberculosis of moderate severity without any visible tendency to spontaneous healing on the one hand and without any likelihood of rapid worsening of their condition or chances for recovery, on the other. The question of whether the excreted bacilli are still sensitive to isoniazid or have already become resistant remains of secondary importance, since, according to the above concept, the new medicament must also be effective in the animal test against tubercle bacilli resistant to isoniazid.

2) *Criteria for the evaluation* of efficacy are to be divided into two groups, the chief ones being sputum conversion and x-ray film findings and the secondary ones: general condition, body-weight, temperature, cough, sputum quantity, blood sedimentation rate, blood count, etc.; the latter are only of minor importance. X-ray film findings should not be evaluated by the attending physician, but by an independent radiologist, experienced in the field of chest diseases.

3) *Number of patients.* For the first, informative qualitative evaluation ("pilot study"), 10 to 15 patients may suffice. The length of treatment with the single preparation to be evaluated must be at least three months.

4) For *a detailed evaluation* of a single medicament which has shown promise in a preliminary study, the treatment of at least 50 to 100 patients is deemed necessary; the type of patient, duration of treatment and criteria for evaluation must correspond to the conditions of the pilot study.

c) Finally, to assess the *value in combined chemotherapy of a new antituberculosis drug recognized to be effective and well tolerated,* two groups of patients are compared clinically, the first receiving isoniazid plus PAS, and the second the new preparation plus PAS. Each group will have to comprise at least 100 patients, and the same criteria are used for the choice of patients and evaluation of the results as described above. The period of treatment, however, will have to be extended to at least six, and if possible nine to 12 months. The combination of isoniazid or the new preparation with PAS is based upon the fact that among the classical antituberculosis agents, PAS possesses the least antituberculosis activity. Thus, the new medicament is practically compared with isoniazid as "standard." For this reason, the combination of the new drug with isoniazid should not be tested comparatively, because the effect of isoniazid alone is so pronounced that any additional effect of the second drug would be unrecognizable or at least difficult to evaluate.

Combinations of three or more antituberculosis drugs should be avoided in this connection, as they make control of the conditions still more difficult. Moreover, no marked increase in efficacy by such means has so far been confirmed, whereas the toxicity is certainly increased.

On the other hand, alternating treatment with various single antituberculosis drugs seems, according to Fust and Heim, to be a method which, in view of the results obtained, deserves serious consideration and re-examination. The single antituberculosis medicaments follow each other every four to six weeks, and the delay in the development of resistance is at least equal to that obtained with simultaneous combined therapy. One of the advantages of this method is the definitely better tolerance for the preparations in alternating single drug therapy compared with combinations.

III. Experimental and clinical evaluation of a few new antituberculosis drugs

1. *Kanamycin*

Results of experimental and clinical trials agree in the main points that the preparation possesses a moderate antituberculosis activity, but is generally poorly tolerated. Kanamycin is half as effective and twice as toxic as streptomycin. According to the aforementioned criteria, it cannot, therefore, be accepted as an antituberculosis agent, except in special cases.

2. *D-Cycloserine*

In animal experiments, this preparation possesses an antituberculosis activity which corresponds to that of kanamycin. Its demonstration is somewhat difficult, because the rate of elimination of D-cycloserine by the smaller rodents normally used in the laboratory is very high, so that effective concentrations of active substance in the body can only be attained under special experimental conditions. D-cycloserine remains much longer in the body of monkeys and, therefore, has a good effect in experimental simian tuberculosis.

Clinical experience with D-cycloserine, on the other hand, gave rise to extensive and lively discussion, the conclusion of which was that D-cycloserine, in the opinion of most of the clinicians participating, is a useful medicament in the treatment of human pulmonary tuberculosis if given in doses of at least 750 mg. daily. Pyridoxine (Vitamin B_6)—about one to three times 100 mg. daily—seems to reduce considerably the frequency and intensity of side effects which have so far limited the maximum dose of D-cycloserine, without influencing its antituberculosis activity (Pult). Piszczek gives D-cycloserine together with pyridoxine, without hesitation, to out-patients also. Even daily doses of up to 2 gm. no longer caused serious side effects.

For years, D-cycloserine was, as a rule, prescribed only when other antituberculosis drugs were of no further help. It is possible that for this reason the full value of the preparation was not recognized, as it was evaluated chiefly on the basis of results in old chronic cases, in which even the "standard" preparation, isoniazid, was not sufficiently effective. When given in recent cases, Hein, for example, says considerably better results can be obtained with D-cycloserine. He further points out the fact that with alternating use of D-cycloserine and isoniazid—sometimes combined with prednisolone—the number of relapses can be definitely reduced and the formation of tuberculomata prevented. Sabar stated that diseases of the lungs caused by different strains of atypical Mycobacteria sometimes responded much better to D-cycloserine than to isoniazid.

So long as no better preparations are available, the field of application of D-cycloserine should be determined more accurately by further observations.

3. *α-Ethylthioisonicotinamide* (1314)

According to Rist *et al.*, the antituberculosis activity of the preparation has been shown experimentally to lie between those of isoniazid

and streptomycin. The minimal effective dose for the mouse, rat or guinea pig amounts to about 10 mg./Kg. The effect increases considerably as the dose is raised from 10 to 20 mg./Kg. The preparation is effective against tubercle bacilli resistant to other antituberculosis drugs, with the exception of the thiosemicarbazones. Its toxicity, in proportion to efficacy, is about double that of isoniazid.

Estimates of the clinical usefulness of the preparation are not unanimous. Its efficacy seems to be limited; Spina considers ∝-ethylthioisonicotinamide alone close in efficacy to PAS given orally and pyrazinamide, but inferior to isoniazid, streptomycin, PAS given intravenously and cycloserine. Its use, however, is greatly impeded by marked gastric intolerance, as pointed out especially by Berg, von Krogh and Spina. This difficulty, which seems to be even more frequent in combined chemotherapy than with the drug alone, consists of pain, lack of appetite, nausea and vomiting and relatively often compels the doctor to suspend administration.

For chemoprophylaxis, for out-patient treatment of mild cases and for maintenance therapy, injectable preparations which can be administered at intervals of one to two weeks are required. Such depot preparations are particularly desirable in countries where medicine and hygiene are still at the beginning of their development.

Finally, the question of cost remains to be considered, since large-scale application of chemotherapy is feasible only when the drugs used are not too expensive.

THE "B" LINES OF KERLEY AND LEFT ATRIAL SIZE IN MITRAL VALVE DISEASE

The radiographic as well as the left atrial catheterization data for 89 patients, including 70 with mitral valve disease, have been studied to determine if any correlation exists between the mean left atrial pressure and the left atrial size or between the mean left atrial pressure and the appearance of the "B" lines of Kerley. No absolute correlation was found between the mean left atrial pressure and the size of the left atrium as judged from the radiographs alone.

There is no constant relationship between the appearance of the "B" lines and the mean left atrial pressure. There were no "B" lines in cases with a mean left atrial pressure below 14 mm. Hg; in the majority of cases with a mean left atrial pressure above 30 mm. Hg, "B" lines were present. As a group, patients with mitral valve disease who show "B" lines have a higher average mean left atrial pressure than those who do not exhibit "B" lines.

Melhem, R. E., Dunbar, J. D., and Booth, R. W.: "The 'B' Lines of Kerley and Left Atrial Size in Mitral Valve Disease," *Radiology*, 76:65, 1961.

CYSTIC FIBROSIS: A COMMUNITY CHALLENGE

The authors review the incidence of fibrocystic disease of the pancreas (mucoviscidosis, exocrinosis). According to reports cited, the incidence calculated in 1946 of cystic fibrosis was 1.73 per 1,000 live births in New York area; in 1958, the estimated prevalence of cystic fibrosis in the United States was 0.7 to 1.7 per 1,000 live births. The data for the Massachusetts area indicate an even greater incidence, as high as 1 in every 600 newborn infants. For the Swiss population, 7.22 new cases per 10,000 births per year were calculated. A national hospital survey of cystic fibrosis indicates that 2,525 persons were hospitalized in the United States in 1957 because of cystic fibrosis, and one out of every six or seven died. The annual number of deaths attributed to this disease during the 1952-57 period ran from 295 in 1952 to 475 in 1955 to 359 in 1957. In the bigger pediatric hospitals, cystic fibrosis may represent 3 per cent of autopsies and 0.2 per cent of hospital admissions.

Kulczycki, L. L., and Macleod, K. I. E.: "Cystic Fibrosis: A Community Challenge," *Public Health Rep.*, 76:85, 1961.

The Surgical Considerations of Bullous Emphysema

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Increasing surgical interest in bullous emphysema has been manifest in recent years. Justification for surgery in many series of cases has been vague but there is more and more agreement on the necessity for considering an increasing number of these patients for surgery. The first American reference on this subject was in 1925 when Koontz reviewed the literature and collected 105 cases. The surgical program was somewhat vague at this early date due to the undeveloped status of resection surgery. By 1937, Schenck had collected 381 cases and presented five of his own. Of these, four were subjected to local excision and one was lobectomized. He remarked that cysts easily herniated from the wound facilitating excision. In fact, he stated that bullae might continue to increase in size with each breath, necessitating opening them to facilitate dissection. Tyson, in discussing this presentation, emphasized the short life expectancy in many of these patients and related a case operated 11 years previously who expired with cor pulmonale.

In 1949, Ravitch and Hardy reported 12 patients and advised surgery as soon as the condition was diagnosed. Ten of their patients underwent lobectomy and one pneumonectomy. This was apparently the ultra-radical approach. By 1950, another group of 14 cases was reported by Samson and Dugan, and in 1952 Crenshaw and Rowles added 11 more. Both of these groups took a more conservative surgical approach, limiting the operation to local excision where possible and thereby conserving lung tissue. Many other significant contributions were made in the literature about this time, namely, Nissen, Head and Avery, Brock, Naclerio and Langer, Albritton and Templeton, and Massie and Welchon.

The cause of bullous emphysema is not completely clear, but there appears to be a loss of elastic tissue in the lung. Certain predisposing causes may be present as a chronic cough, from repeated infections, spasm, or occupational hazards, or the condition may be secondary to chest wall changes. Many terms have been applied to the disease: blebs, bullae, tension cysts, air cysts, bullous emphysema, pneumatocele, and "vanishing lung." More important than the designation is the extent of involvement. This may not be fully apparent until lung function studies give some clue and actual thoracotomy reveals the true nature and extent of the process. Bullae may be uniloculated or multiloculated. They may be segmental in distribution or completely unanatomical in location. Frequently a group of pea sized blebs may be seen along fissure borders which is not discernible in roentgenograms. The capsule of the bulla is thin and translucent with many areas of fibrous thickening. On opening larger bullae, one sees many loose strands of connective tissue, lung substance and denuded vessels traversing the spaces. These may be so numerous and lacy as to resemble cotton candy, a term frequently applied to the diffuse category. Many bullae communicate with

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TABLE 1—PREOPERATIVE DATA

Age:	23 to 67	20	30	40	50	60
		4	10	9	3	3
Race:		White—18			Colored—11	
Side:		Right—10		Left—15		Bilateral—3
Lobar-segmental types:			18			

each other and bronchial openings may be numerous. Some bullae regress spontaneously, but many others undergo serious complications as spontaneous rupture and even abscess formation. Spontaneous pneumothorax may occur several times before decision for thoracotomy is reached. If the disease is allowed to continue in an advanced state, chronic cor pulmonale results. Such patients live in a state of dyspnea for many years with altered blood carbon dioxide and reduced hemoglobin content resulting from the stagnant air within large areas of nonfunctioning lung. Many of these patients present medical failures and many have been treated for asthma. Since the formation of bullae is associated with varying degrees of bronchospasm, wheezing is not an uncommon symptom. Such focal obstruction may also lead to areas of bronchiectasis, pneumonitis and even abscess. Animal experiments have shown that prolonged bronchial obstruction leads to irreversible emphysema.

The indications for surgery and removal of space-occupying bullae may be clearer in some patients than others. A patient presenting a spontaneous pneumothorax for the first time with no roentgenographic evidence of bullae or blebs may be treated conservatively with the assumption that there is a small bleb present which may be incased in adhesions after the lung has re-expanded and may never rupture again. Such assumptions are erroneous when such patients suffer a recurrence of their pneumothorax. We have now adopted the following criteria for surgery:

1. Repeated pneumothorax with ruptured bleb as the cause.

2. Discovery of a large bulla in roentgenograms with or without pneumothorax. This may be bilateral and sufficient intervening lung must exist. Removal of these bullae safeguards against rupture, removes degenerated lung containing "dead" air, removes compression from adjacent normal lung, and may reduce bronchospasm and help decrease incidence of infection. Such accomplishments may actually prolong life.

TABLE 2—PREOPERATIVE SYMPTOMS

Dyspnea		11
Pain		7
Asthma		7
Hemoptysis		6
Pneumonia		2
Coin lesion		2
Abscess		1
Pneumothorax		
1 attack	6	
2 attacks	5	
3 attacks	2	13

TABLE 3—OPERATION TYPE

Excision bullae large	12
moderate	11
Segmentectomy	3
Lobectomy	3
Lung denervation	5
None—cotton-candy lung	2

3. Dyspneic states or asthma in bullous patients which is interfering with normal living.

4. Chronic infection, either as repeated pneumonitis, bronchiectasis, or abscess formation.

Due to the progressive nature of many of these cases, all patients with suspected bullae should have careful screening. This should include bronchoscopy which frequently reveals the twisting and distortion of bronchial orifices in many parts of the lung hitherto unsuspected, or may even reveal the presence of long-standing obstructions. Lung function studies may give some clue as to the amount of both good and destroyed lung. A cardiac evaluation may be needed in long-standing cases. Many patients are acute problems and are admitted with tension pneumothorax. In these, relief of the pneumothorax is essential before evaluating the extent of the disease. Lung function studies done in face of extensive pneumothorax gives a tracing which may be of little value.

Treatment of this condition should be essentially surgical. There are a few conservative measures which will be mentioned only to be condemned. These consist in injecting some caustic agent as silver nitrate solution, hypertonic glucose or iodized oil into the pleural space to promote adhesions. Some authors advocated needling the bulla to decompress, and while this may be successful at times in children, there is some risk to the procedure. Decompression is not entirely physiological, for although the cysts may collapse, their walls will not adhere to one another, and many may continue as fistulae. In addition to these, certain compression measures have been advocated to reduce the residual capacity of the thorax, as pneumoperitoneum and abdominal belts. They are of little value in any but the diffuse types of emphysema.

Resection is the ideal method and it should be done to remove only the pathological lung and a minimum of parenchyma. Patients do better as soon as the chest is open, showing dead space reduction and allowing uninflated lung to expand. The loose sac is excised after opening the bulla, and the underlying area of the lung is closed with a continuous

TABLE 4—POSTOPERATIVE DATA

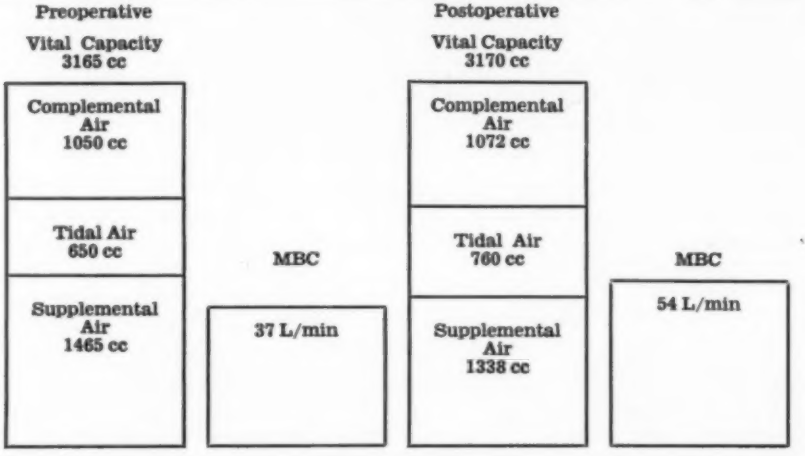
Working		16
No symptom		8
Dyspnea slight		10
moderate		4
severe		4
Chest pain		3
Pneumonia		1
Recurrent pneumothorax		0
Dead		3
PO—1	Cor pulmonale—2	

catgut suture, eliminating pocketing and preventing air leaks. The decision of how deep into the lung one should excise is not always easy and one may prefer to leave some collateral areas rather than incorporate too much intervening good lung in the excision. The normal lung is allowed to expand and many previously compressed areas will now be functioning. Some authors have advocated removal of parietal pleura to facilitate fusion of the lung with the chest wall and promote collateral circulation. We have felt that creation of chemical irritation to the pleura with powdered talc has produced excellent adhesions, and in a few cases only a mechanical rubbing with gauze is used. Dusting the pleura is not essential but adds a little security in trapping small inaccessible blebs so they cannot rupture. In some cases, the disease is anatomically located so that it may be more feasible to remove an entire segment or a lobe. Failures in resection surgery result from the diffuse cotton candy type of lung, but even some of these patients are improved by removing adjacent bullae and leaving the cotton candy undisturbed.

Denervation of the lung should be considered in patients with a complaint of severe wheezing. Although technics may differ, most should include both sympathetic and vagal fibres surrounding the lung root as described by Klassen. It would appear that some cases have less bronchospasm after denervation and it adds little to the operating time.

Postoperatively, one should obtain quick and complete expansion of the operated lung by continuous underwater suction. Oxygen therapy may be necessary, but often times the patient is in a better respiratory state after surgery than before. One must always be alert to contralateral pneumothorax, particularly in cases having bullae on the unoperated side. If such spontaneous pneumothorax occurs, tube drainage is essential and we now believe that such patients should be taken back to surgery and the other lung bullae remedied without delay. We lost one

TABLE 5—COMPOSITE STUDY OF 9 PATIENTS PRE- AND POSTOPERATIVELY
(MBC=maximum breathing capacity)



such patient by relying on intercostal tube suction when it failed to expand the lung.

We have operated on 29 of these cases. There was one postoperative death. Two others have died in the years involving this study, both with cor pulmonale. All of these cases were seen between 1950 and 1958 and none has been under observation less than two years.

Eighteen were white and 11 colored. Ages varied from 23 to 67 with the majority in the third and fourth decades. Symptoms and findings leading to surgery varied from dyspnea in 11 to repeated pneumonitis in two. Of interest were 13 who had spontaneous pneumothorax of whom seven had more than one episode. Hemoptysis occurred in six and two were operated for suspected "coin" lesions. The left side was involved 15 times and the right 10 times; three were bilateral. The involvement was found to be lobar or segmental 18 times (see Tables 1 and 2). Types of surgery depended largely on distribution: 23 had excision of the bullae; three had segmental resections, and three had lobectomy. In two, nothing was done because of diffuse cotton candy findings. Five patients received denervations of the lung with histories of severe asthmatic breathing (Table 3). The results from a symptomatic standpoint can be seen in Table 4. Nine patients had comparative spirometric evaluations which were evaluated conjointly (Table 5). One notices a decrease in supplemental air and a definite increase in maximum breathing capacity which indicated some relief of obstructive states.

SUMMARY

Twenty-nine surgical cases of bullous emphysema are reviewed which have been treated in the last eight years.

The most apparent effect of surgery was on symptomatology. Sixteen of the original 29 cases are alive and apparently well. One died after surgery and two others died later. Many of the remainder, though somewhat dyspneic, are definitely improved. None has had recurrence of pneumothorax.

RESUMEN

Veintinueve casos quirúrgicos de enfisema buloso tratados en los últimos ocho años se revisan.

El efecto mas aparente de la cirugía fué sobre la sintomatología. 16 de los originales 29 están vivos y aparentemente bien. Uno murió después de la operación y dos mas tarde. Muchos de los que quedan aunque algo disneicos claramente han mejorado. Ninguno ha tenido recurrencia de neumotórax.

RESUMÉ

29 cas d'emphysème bulleux traités chirurgicalement dans les huit dernières années sont étudiés par l'auteur.

L'effet le plus apparent de la chirurgie eut lieu sur la symptomatologie. 16 des 29 cas originaux sont en vie et apparemment en bonne santé. L'un mourut après l'operation et deux autres plus tard. Beaucoup de ceux qui survécurent, encore que dyspnéiques, sont nettement améliorés. Aucun n'a eu de rechute du pneumothorax.

ZUSAMMENFASSUNG

Bericht über 29 chirurgisch behandelte Fälle von bullösem Emphysem, die in den vergangenen 8 Jahren behandelt wurden.

Der am meisten augenfällige Effekt war ein symptomatischer. 16 der ursprünglichen 29 Fälle sind am Leben und fühlen sich wohl. Einer starb nach der Operation und 2 starben später. Viele der übrigen Kranken haben sich eindeutig gebessert, obwohl noch bis zu einem gewissen Grad Kurzatmigkeit besteht. In keinem Fall war der Pneumothorax wieder aufgetreten.

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BACTERIAL DRUG SUSCEPTIBILITY

The *in vitro* susceptibility of bacteria to the drugs tested over a four-year period was evaluated. The percentages of *Staph. aureus* that were susceptible, in decreasing order, were: chloramphenicol, 87 per cent; nitrofurantoin, 85 per cent; erythromycin, 52 per cent; neomycin, 40 per cent; tetracycline, oleandomycin and novobiocin-penicillin, 33 to 36 per cent; oxytetracycline, 30 per cent; streptomycin, 27 per cent; and penicillin and novobiocin, 19 per cent.

The percentages of *Streptococcus hemolyticus* that were susceptible were: chloramphenicol, 85 per cent; nitrofurantoin, 76 per cent; penicillin, 77 per cent; tetracycline, 64 per cent; erythromycin, 58 per cent; oxytetracycline, 55 per cent; streptomycin, oleandomycin and novobiocin-penicillin, 50 to 52 per cent; neomycin, 40 per cent; and novobiocin, 9 per cent.

The percentages of *D. pneumoniae* that were susceptible were: chloramphenicol, 85 per cent; nitrofurantoin, 68 per cent; tetracycline, 59 per cent; oxytetracycline, 53 per cent; penicillin, 51 per cent; streptomycin, 47 per cent; erythromycin, neomycin, oleandomycin and novobiocin-penicillin, 39 to 40 per cent; and novobiocin, 17 per cent.

The percentages of *A. aerogenes* that were susceptible were: nitrofurantoin, 74 per cent; chloramphenicol, 71 per cent; tetracycline and oxytetracycline, 47 per cent; erythromycin, 38 per cent; neomycin, 33 per cent; oleandomycin and novobiocin-penicillin, 28 to 29 per cent; and novobiocin and streptomycin, 22 per cent.

The percentages of *Proteus* that were susceptible were: nitrofurantoin, 77 per cent; chloramphenicol, 56 per cent; neomycin, 41 per cent; oxytetracycline and oleandomycin, 39 per cent; novobiocin-penicillin, 37 per cent; tetracycline, 33 per cent; erythromycin, 31 per cent; and novobiocin, 12 per cent.

The percentages of *Ps. aeruginosa* that were susceptible were: chloramphenicol, 79 per cent; nitrofurantoin, 70 per cent; polymyxin B, 68 per cent; novobiocin-penicillin, 16 per cent; and neomycin, 10 per cent.

The percentages of *H. influenzae* that were susceptible were: chloramphenicol, 93 per cent; nitrofurantoin, 79 per cent; tetracycline, 62 per cent; oxytetracycline, 54 per cent; erythromycin, 49 per cent; penicillin, novobiocin and novobiocin-penicillin, 44 to 45 per cent; oleandomycin, 42 per cent; and streptomycin, 40 per cent.

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Pulmonary Hydatidosis*

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"When the liver is filled with water and bursts into the epiplöon, in this case the belly fills with water and the patient dies."—Hippocrates, 55th aphorism, Sect. VII.

This is probably the earliest reference to hydatid disease, a parasitic infestation which, at times, threatens to disturb the equilibrium of community life in certain South American countries and elsewhere.

It should be stated at the outset that hydatid disease represents the cystic or larval stage in the life-cycle of the tapeworm *Echinococcus granulosus* (Batsch, 1786), which is normally a parasite of the small intestine of the dog, its definitive host. The adult *Echinococcus* is 3-6 mm. long with a pyriform scolex at the anterior end. The scolex bears four discoid suckers and a rostellum which is surmounted by 28-50 chitinous hooklets.

In the terminal segment, the uterus with its lateral evagination contains from 3,000 to 5,000 ova. When the terminal proglottides mature they are shed and expelled with the faeces. Then, either singly or en masse, they may be ingested in contaminated food or water by the intermediate host in whom larval development takes place. The ova, following ingestion, hatch in the duodenum. The chitinous embryophore in which each is invested is dissolved and releases the hexacanth embryo or onchosphere which bores its way through the intestinal mucosa into the mesenteric venules and then, by embolic spread, becomes lodged in the capillary plexuses of various tissues and organs. Although mononuclear leucocytes attack the embryos at the sites at which they lodge and undoubtedly destroy many of them, those that survive begin to grow and by the fourth day have developed a cystic cavity. After three weeks, the young cyst is 250 μ in diameter and the host's tissue reaction is conspicuous. Four months later, the cysts, now known as hydatids, have become differentiated into two layers, viz. a chitinous laminated and non-nucleated ectocyst and an internal nucleated germinal layer or endocyst. From the germinal layer there are produced, by gemmation, masses of cells which become petiolated and vacuolated to form brood capsules. These either remain fixed to the parent cyst or become free to float within the cavity as endogenous cysts. Exogenous cysts are formed by the extrusion of a portion of germinal epithelium through a weakened or traumatised area in the hydatid capsule. From the inner surface of the brood capsule, scolices develop and invaginate so that their developing rostellum and hooklets appear to be inside the scolex (Figure 1). Each brood capsule may produce up to one dozen scolices and there may be as many as a thousand within a single cyst. The young scolex remains in the invaginated condition until ingested by the final host, within whose alimentary tract it evaginates and grows by strobilation into an adult tapeworm.

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Distribution of Echinococcosis

As a direct result of the cosmopolitan nature of the dog, hydatid disease is known in practically every country, and where the inter-relation of dog and sheep is well established, it is particularly abundant. Dogs infected by feeding on the offal of condemned sheep are the chief source of human infection. Hence, it is found that the most extensive and intensive endemic regions are those of the sheep raising countries, notably Australia, Argentina, Uruguay and Paraguay. In the British Isles, the disease is rare, but occurs not infrequently in South Wales. Although autochthonous cases are rare in the United States, hydatid disease is frequently reported among immigrants, especially from the Middle East.

The Genesis of Lung Hydatids

As has been mentioned above, the embryos reach the capillary plexuses of the various tissues and organs by embolic spread. The majority (c. 70 per cent), carried by the portal circulation become lodged in the hepatic capillaries and develop into primary hydatid cysts of the liver. The size of the embryos is so small, however, that a few may pass through the hepatic circulation and thus reach the pulmonary network of fine vessels. Very few of these manage to negotiate this second barrier, but those that do are carried to the peripheral organs, their ultimate fate depending on the vagaries of the circulation. Infection is commonly acquired during childhood and the development of the cysts is insidious and unspec-

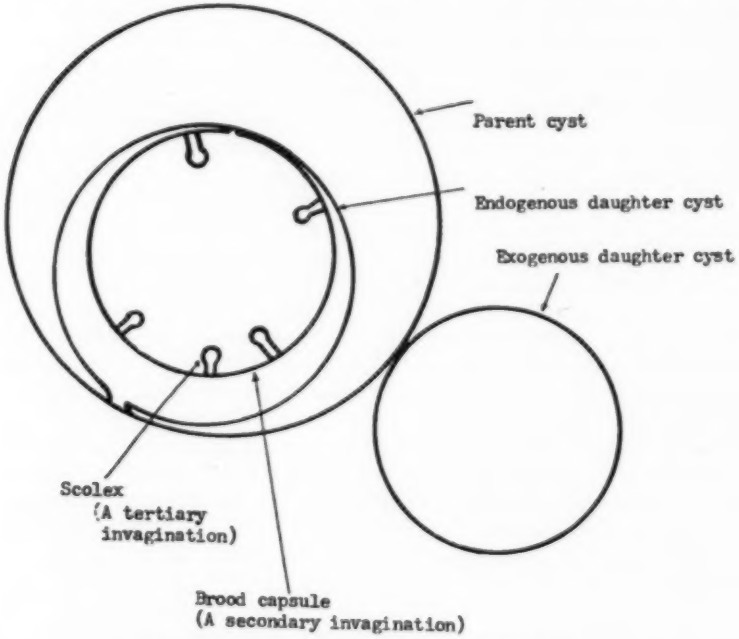

FIGURE 1: Diagram of typical hydatid cyst.

tacular. As the young cyst grows there is a well-marked tissue response from the host in which there is hyperaemia and a proliferation of connective tissues, epithelioid cells, eosinophils and foreign body giant cells. The surrounding lung tissue undergoes pressure atrophy and fibrosis which results in the formation of a distinct adventitious capsule of variable development.

Hydatid cysts grow well in lung tissues as these offer little resistance to spread. Depending on its site within the lung a hydatid may grow to a very large size before symptoms develop. It has been possible to measure the rate of growth radiologically and Edwards (1926) found that one cyst increased from two to three inches in diameter in one year. The largest recorded cysts are between 20-30 centimeters in diameter. Laennec described the case of a small girl who died from bilateral giant cysts which almost filled each hemithorax. The right lung is, on account of its greater circulation, more frequently affected than the left in the proportion 65:35 (Dew, 1928). Usually the bases are affected rather than the upper lobes but apical cysts and multiple primary cysts have been recorded. As the cysts enlarge they do not infiltrate the bronchi or destroy them and in this capacity differ from malignant neoplasms and tuberculous processes. The cysts will, however, displace the bronchi and compress blood vessels. Beaumont, (1950) describes the case of a large hydatid of the left base which eroded through the descending aorta to form a false aneurysm. Erosion of the ribs and vertebrae has also been described.

Secondary Pulmonary Hydatids

These are derived from brood capsules or scolices which are in turn derived from primary cysts.

(a) Metastatic cysts: These are the commonest variety and are due to vascular leakage of hydatid elements from a primary cyst situated on the venous side of the circulation. The pulmonary arteries are responsible for the final dissemination of the hydatid elements within the lungs. Barrett and Thomas (1952) describe a case in which a cyst of the right ventricular wall ruptured and resulted in the seeding of numerous secondary lung hydatids. Escudero and Finochietto (1922) describe another case in which traumatic rupture of a liver cyst resulted in secondary peritoneal and pulmonary hydatids.

(b) Intrathoracic extension from other sites: The intrathoracic extension of hepatic cysts through the diaphragm is well-known, but intrathoracic extension from spleen, kidneys and vertebral column have all been recorded. In patients in whom the diaphragm is naturally fenestrated or weakened the extension of a liver cyst into the thorax is unspectacular. In other cases there may be a fistulous connection between a suppurating liver hydatid and the pleural cavity with empyema formation. More commonly there is simple erosion of the diaphragm with extrusion of the cyst into the thorax.

The Fate of Lung Hydatids

(a) Aseptic death and degeneration: Death of a cyst may occur at any time and may result from rupture or the entry of micro-organisms.

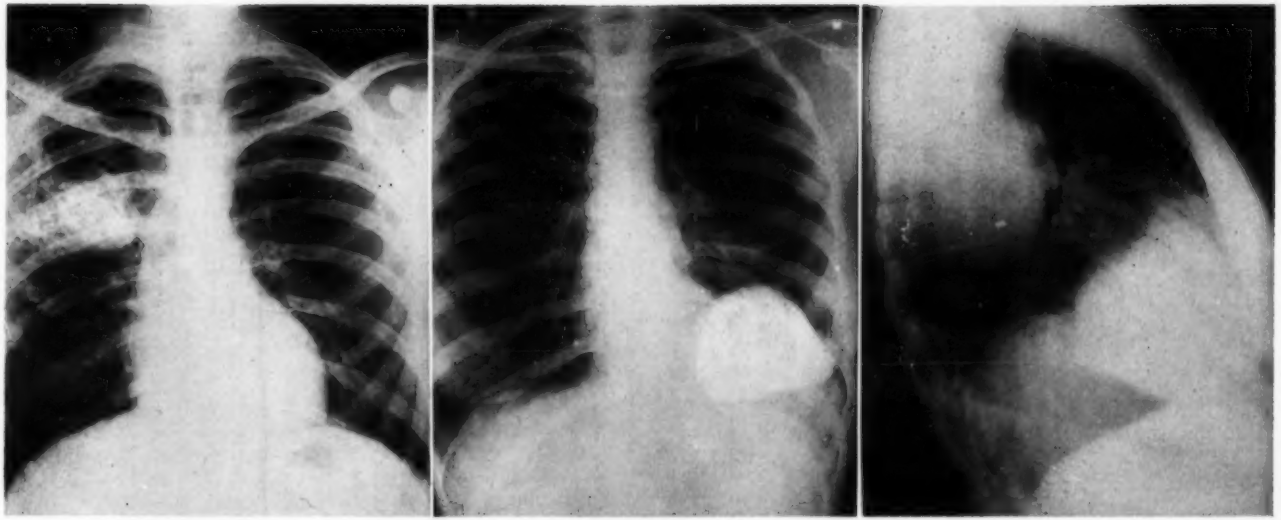

FIGURE 2 FIGURE 3 FIGURE 4

FIGURE 2: Postero-anterior x-ray film showing hydatid cyst at base of right upper lobe. FIGURE 3: Postero-anterior x-ray film showing hydatid cyst at base of left lower lobe. FIGURE 4: Lateral x-ray film showing five hydatid cysts in right lung.

Cysts have been known to live for 40 years but this is exceptional. The most common cause of death is failure of nutrition as dictated by structural changes in the adventitia. As age advances the adventitious capsule becomes more densely fibrous and less vascular. Calcification then follows and its permeability decreases. This results in the deprivation of a food supply and the aseptic death of the cyst.

(b) Rupture of a cyst: Partial rupture will result in the slow leakage of hydatid fluid from the cyst. Complete rupture on the other hand usually terminates the life of the cyst and may prove fatal to the patient. Rupture into a bronchus may be initiated by a bout of coughing, in which case the contents of the cyst may be expectorated or more rarely cause fatal asphyxia. Sub-pleural cysts may rupture into the pleural cavity and if a bronchus is also involved a hydatid pneumothorax is formed.

(c) Infection of lung hydatids: Because of the integrity of the constituent hydatid membranes it is doubtful whether micro-organisms can enter an intact cyst. If partial rupture of the cyst occurs entry of the organisms is facilitated. The adventitia becomes thickened by inflammation and a pyogenic membrane appears on its inner surface. Sometimes adequate drainage is supplied by a bronchus and the patient relates a history of expectorating quantities of evil tasting sputum. Terminally empyema or pyopneumothorax develops.

Hydatid Disease and Anaphylaxis

It is probable that during the life of a hydatid varying quantities of hydatid fluid are absorbed by the host with the result that specific sensitisation occurs. If, subsequently, rupture or leakage occurs, anaphylactic phenomena may result. Cardiac disturbances, dyspnea, pruritus, cough, agitation and sweating are common symptoms. Originally these phenomena were thought to be due to reflex action and later were attributed to the primary toxicity of hydatid fluid (Roy, 1887). More recently the work of Bacigalupo and Grassi (1922), Guisti and Hug (1922) and Bryce, Kellaway and Williams (1924) has retreived the situation from obscurity and thrown fresh light on the pharmacology of hydatid fluid. The absorption of hydatid fluid takes place most readily during the early stages of cystic development before fibrosis of the adventitia occurs. The close resemblance of these phenomena and those associated with anaphylaxis due to foreign proteins, coupled with the fact that patients with hydatid disease show sensitivity to hydatid fluid injections and that their sera has precipitating and complement fixing properties, makes it almost certain that most of the symptoms are attributable to anaphylaxis.

Diagnosis of Pulmonary Hydatidosis

Since hydatid cysts take many years to develop before their presence induces symptoms upon which a diagnosis can be made, it is usual to encounter the disease in an advanced state of progress. There appears to be no special symptom characteristic of hydatid disease, those produced being due to a space occupying lesion causing pressure upon adjacent structures. Most patients present with a history of cough and occasionally with haemoptysis. There may be a dull chest pain that has persisted

for years, and some patients are breathless, their dyspnoea being due to pressure on the bronchi. Frequently a patient presents after an episode of coughing during which portions of the hydatid membrane are expectorated, causing considerable alarm. Physical signs are often minimal. Inspection may reveal bulging of the ribs with a localized increase in intercostal width. Percussion may reveal an area of dullness over the cyst and auscultation may reveal diminished air entry to the same area. The occurrence of cough, hemoptysis and varying pulmonary signs commonly lead to a diagnosis of tuberculosis, neoplasm, etc., especially when the cyst is situated in the upper lobe of a lung. It is important to inquire as to whether the subject has lived in a place where the disease is endemic and to determine whether he has come in contact with dogs or sheep during that time.

Radiography is important as it localizes a cyst accurately. Because of the high saline content of hydatids characteristically sharp shadows are seen, commonly spherical in outline (Figures 2, 3, and 4), and there may be calcification of the walls. As a rule neoplastic growths are denser than hydatids and tend to mask the rib shadows to a considerable extent. Other investigations include examination of the differential blood picture which, during the early stages of cystic development, may reveal an eosinophilia.

Serological Tests for Hydatid Disease

1) Casoni test: Tomaso Casoni (1911) first made use of the fact that patients with hydatid disease become sensitised to hydatid fluid, to invent the intradermal test which today is known by his name. So effective is this test that Pontano (1921) and Serra (1920) in a test series obtained 84 per cent and 90 per cent of positive results. The test consists of the intradermal injection of sterile purified hydatid antigen. Within ten minutes there will be an immediate response in the form of a raised wheal which fades after about one hour. Six hours later there is a delayed response consisting of a localised area of oedema with a transitory erythema. The test will give false positives if the patient is jaundiced, syphilitic, has urticaria factitia or has at any time harbored a tapeworm other than *Echinococcus* sp.

2) Precipitin reaction: Fleig and Lisbonne (1907) first utilized the fact that absorption of hydatid fluid results in the formation of a serum precipitin, to evolve the standard precipitin reaction. The test is difficult to perform because it is not easy to prepare standardized hydatid antigen.

3) Complement fixation test: The principle of the Bordet-Gengou test was first applied to hydatid disease by Ghedini in 1906.

The test is specific and relies on the presence of specific hydatid antibody in the serum of patients who have absorbed hydatid antigen. This antibody in the presence of specific antigen combines with normal complement and the latter cannot be demonstrated by means of a sensitized system utilizing red blood cells and specific hemolysin. This test is sensitive and not anti-complementary and does not appear to give false positives.

The Treatment of Pulmonary Hydatids

It must be stated at once that there is no therapeutic or medical treatment for lung hydatids and in general operative surgery must be resorted to. Aspiration of the cysts is a dangerous procedure, still carried out on the continent, and may prove fatal due to sudden anaphylaxis.

In 1952, N. R. Barrett and Dillwyn Thomas described their operation for the removal of simple hydatid cysts. The patient is prepared for thoracotomy and the lung exposed. The infected lobe is enclosed within a black mackintosh bag which has strings for gathering up the inlet. The strings are pulled tight around the hilum, but must not impede the respiration or circulation of the lobe. The bottom of the bag is cut open and brought out through the incision so that the infected part is enclosed within a waterproof container. This is to prevent the spill-over of living hydatid elements, the black material facilitating the detection of the white scolices. The exact site of the cyst is now determined and the lung is incised along an intersegmental plane over the cyst and down to the adventitia. The adventitia is now incised over the lower half of the cyst with a straight cut. The cyst will try to herniate itself out of the lung, a fact which is of considerable help to the surgeon. It is of great importance to avoid touching the laminated membrane of the cyst as it is extremely friable, and on no account should it be grasped with toothed instruments. The anesthetist is now responsible for the final expulsion of the cyst from the lung. He steadily increases the pressure of the circulating gases and the hydatid is slowly extruded from the lung intact. As the cyst is extruded the patient is tilted to facilitate its removal and a suitable container is held ready for its reception. No attempt should be made to assist removal with instruments, and in cases of obstinacy a pair of gauze swabs should be sufficient to guide progress.

The residual space is closed by a series of purse string sutures, any patent bronchial fistulae being closed first.

With infected hydatids the problem is to cure a patient suffering from a chronic lung abcess in which the disintegrating laminated membrane constitutes a persistent sequestrum. Lobectomy is the treatment of choice and is essential if the patient is to avoid chronic generalized pulmonary suppuration.

SUMMARY

1. Hydatid disease represents the development of the cystic or larval stage of the tapeworm, *Echinococcus granulosus* (Batsch), within the human body.

2. The disease manifests itself most commonly in the liver with the lungs second in frequency.

3. The diagnosis of hydatid disease presents several problems and since patients may become sensitized to their own hydatid fluid, the Casoni reaction was developed as a specific diagnostic test.

4. Because the disease is irreversible, surgery represents the only treatment. An operative procedure for the removal of pulmonary hydatids is described.

RESUMEN

1. La enfermedad hidatídica corresponde al desarrollo de estado larvado o quístico de la *equinococus granulosus* (Batsch) dentro del organismo humano.

2. La enfermedad se manifiesta más comúnmente en el hígado siendo los pulmones el segundo lugar por la frecuencia.

3. El diagnóstico de hidatidosis ofrece varios problemas y como el enfermo se sensibiliza a su propio líquido hidatídico, la reacción de Casoni se ha constituído en la prueba diagnóstica.

4. Puesto que la enfermedad no es reversible, la cirugía ofrece el único tratamiento. Se describe un procedimiento quirúrgico para la extirpación de las hidátides pulmonares.

RESUMÉ

1. La maladie hydatique représente le développement de l'état kystique ou larvaire du taenia *Echinococcus granulosus* (Batsch) dans le corps humain.

2. L'affection se manifeste le plus souvent au niveau du foie et ensuite dans l'ordre de fréquence aux poumons.

3. Le diagnostic de maladie hydatique pose plusieurs problèmes. Comme les malades peuvant se sensibiliser à leur propre liquide hydatique, la réaction de Casoni s'est imposée comme un test spécifique pour le diagnostic.

4. La chirurgie représente le seul traitement étant donné que l'affection est irréversible. L'auteur décrit un procédé opératoire pour l'exérèse des kystes hydatiques pulmonaires.

ZUSAMMENFASSUNG

1. Die Hydatiden-Krankheit bedeutet die Entwicklung des Zysten- oder Larvenstadiums des Hundebandwurms, *Echinococcus granulosus* (Batsch), im menschlichen Körper.

2. Die Krankheit tritt für gewöhnlich in der Leber auf, die Lunge steht an zweithäufigster Stelle.

3. Die Diagnose der Hydatidenkrankheit stellt verschiedene Probleme, und nachdem Patienten gegen ihre eigene Hydatiden Flüssigkeit sensibilisiert werden können, wurde die Casoni-Reaktion entwickelt als ein spezifischer diagnostischer Test.

4. Da die Krankheit irreversibel ist, besteht die einzige Behandlungsmöglichkeit in operativem Vorgehen. Beschreibung einer Operationsmethode zur Entfernung von pulmonalen Hydatiden.

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Giant Cell Carcinoma of the Lung: Cytological Study of the Exfoliated Cells in Sputa and Bronchial Washings

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In the classification of primary tumors of the lung, one variety is described as a "giant cell carcinoma."[1-3] All the cases in the literature were reported as highly malignant, anaplastic and undifferentiated types of tumors, composed mainly of "loose" multinucleated cells filling the alveolar spaces.

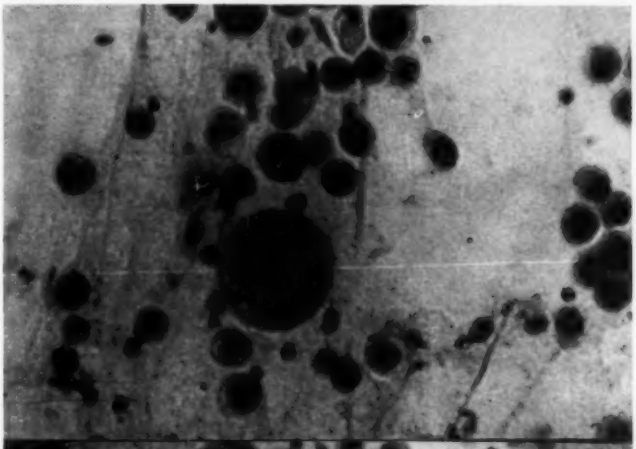

Figure 1

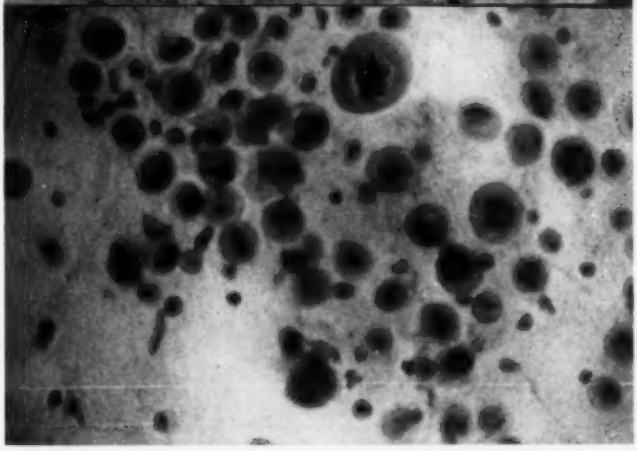

Figure 2

FIGURE 1 (Case 1): Bronchial washing smear with numerous "loose" malignant cells. Note the round multinucleated, hyperchromatic cell (X-430). FIGURE 2 (Case 1): Malignant cells in smear from a sputum with a cell in abnormal mitosis (X-430).

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In the past year, at the University of Maryland Hospital, we had two such cases of atypical giant cell tumors of the lung from which repeated cytological studies of sputa and bronchial washings were examined. The bizarre cells seen were very abundant in all the material submitted, but due to some of their unusual and different aspects, which will be discussed later, their interpretation was difficult and subject to divergent diagnosis between different cytopathologists.

Case Reports

Case 1 (No. 174-1-97 U.H.): In this 45-year-old white man, an area of consolidation in the right upper lobe of his lung was found on a routine chest x-ray film. He then gave a history of having a cold recently, followed by blood-streaked sputum. Physical examination revealed a dull percussion note and moist rales over the posterior segment of the right upper lobe. The cardiovascular system was within normal limits. The examination of his abdomen showed that the liver edge was 4 cm. down the coastal margins. No other organ or mass was felt. His temperature was normal and the white blood count was only slightly elevated. Multiple roentgenograms of the chest demonstrated a consolidation of the right upper lobe of the lung compatible

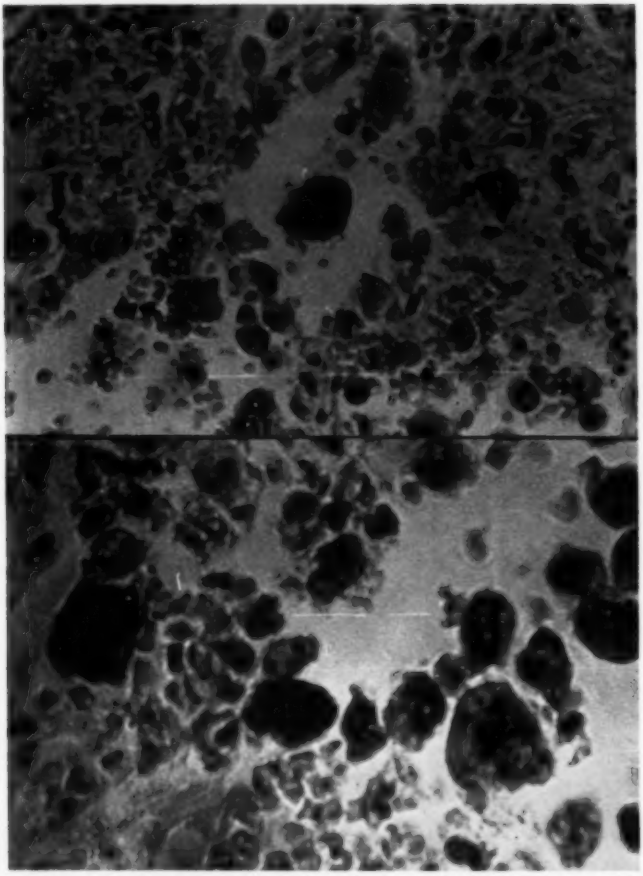

FIGURE 3 (Case 1): Section of the metastasis to the brain. Note the similarity of the cells to the ones exfoliated from the primary lesion of the lung (X-300). FIGURE 4 (Case 1): Section of the brain metastasis showing the marked polymorphism of the cells and their difference of size (X-300).

with a carcinoma or pneumonitis. This picture subsisted during all his hospitalization in spite of the energetic antibiotic treatment that he received. Repeated bronchoscopic examinations were essentially negative. All the segmental bronchial orifices were normal in appearance except for the presence of some orange purulent secretion which was aspirated for cytological examination. In total, two bronchial washings and aspirations and three fresh sputa were examined. All of them showed abundant bizarre single cells (Fig. 1 and 2) which will be described later. All the smears were reported as highly inconclusive. The possibility that the abnormal changes seen in the cells were of inflammatory origin could not be excluded. A needle biopsy of the lungs showed fibrosis, and atelectasis and a cervical lymph node biopsy showed no malignancy. One month later he developed severe frontal headaches. An arteriogram and pneumoencephalogram was read as follows: Metastatic neoplasm to the left parietal occipital and pontine area. Two weeks later he was found in a stuporous state with right hemiparesis. Left parietal occipital craniotomy was done and a small metastatic carcinoma consisting of very anaplastic undifferentiated cells was found (Fig. 3 and 4). He died shortly after. No autopsy was obtained. The entire course of his disease lasted four months.

Case 2 (No. 18-77-50): This 67-year-old white man was admitted for evaluation of his complaint of hemoptysis for about a week before admission. He had a dry cough for the past few years and was a heavy smoker. He denied any chest pain or discom-

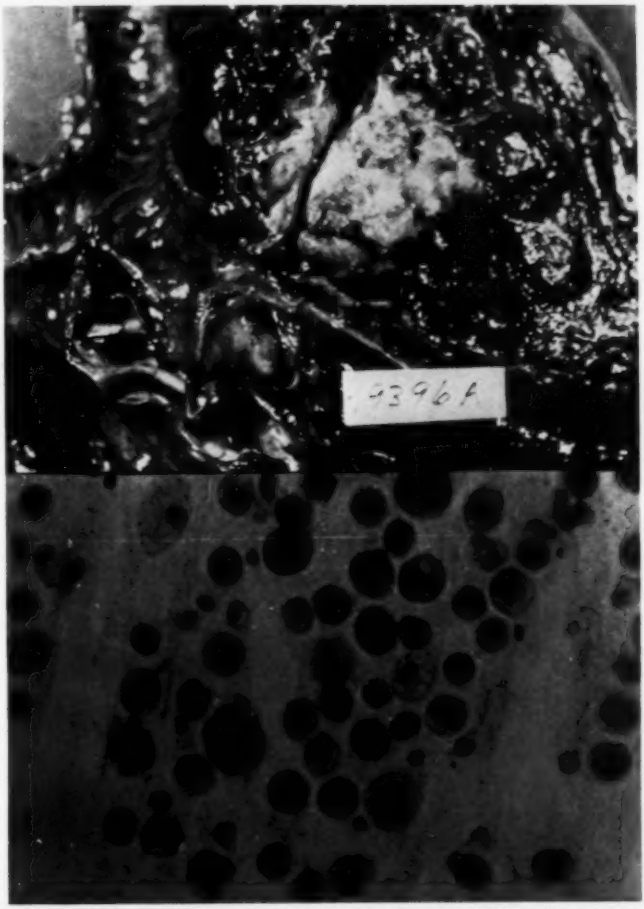

FIGURE 5 (Case 2): Neoplastic mass seen at autopsy in the right upper lobe. Note its extension and relation to the main bronchus. FIGURE 6 (Case 2): Exfoliated malignant cells in smear from a bronchial washing. Note the similarities of these cells to the ones seen in the previous case (Fig. 1) (X-430).

fort. There was no weight loss or loss of appetite. The x-ray film of his chest showed extensive infiltration of the upper lobe of the right lung, probably of inflammatory nature. His temperature was normal. There were rales throughout the entire chest area except for the left upper field. The abdomen was essentially negative. A bronchoscopic examination revealed that the carina was deviated to the right and the orifice of the right upper lobe bronchus narrowed. A total of two bronchial washings and five morning sputum series were examined. All of this material contained an abundant amount of marked bizarre single cells (Fig. 5). Based partially on the experience gained with the first case, the smears were called positive for very undifferentiated malignant cells. The patient's condition rapidly deteriorated. He became weak, and his temperature went up to 103 degrees. A neurological consultation gave the impression of a lesion in the temporal lobe. His condition became worse, he went into a coma and expired 40 days after the first episode of hemoptysis. An autopsy was performed and showed a carcinoma of the upper lobe of the right lung with metastases to hilar lymph nodes, pleura and right temporal lobe of the brain. The right upper lobe bronchus had a thickened wall and was surrounded by a large, tan, firm tumoral mass about 6 cm. in diameter with a friable cut surface (Fig. 6). The lumen of the bronchus was narrowed, but at gross examination, no apparent involvement of the bronchial mucosa by the tumor was seen.

The microscopic image of both tumors is essentially the same (Fig. 7 and 8). They infiltrate diffusely the lung parenchyma leaving the main architecture fairly intact. The majority of the alveolar septa are recognizable in spite of the large amount of malignant cells found in their chambers. The tumor is mainly composed of hyperchromatic cells, usually single, multinucleated and well preserved with marked varia-

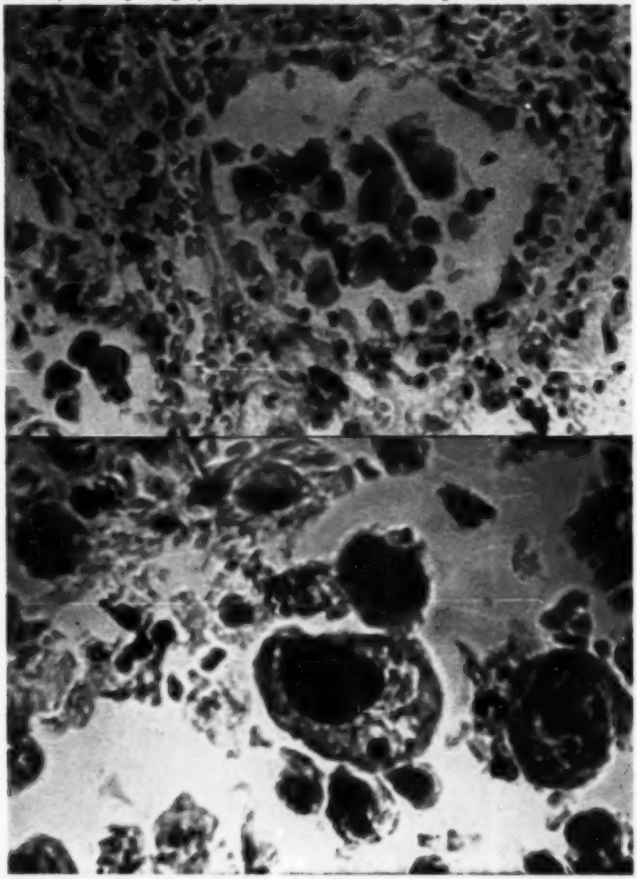

FIGURE 7 and 8 (Case 2): Sections of the primary tumor of the lung. Note the "loose" malignant cells filling the alveolar chambers but respecting the main pulmonary architecture (X-300).

DIFFERENTIAL CHARACTERISTICS OF HISTIOCYTES FROM THE EXFOLIATED CELLS OF A SQUAMOUS CARCINOMA AND GIANT CELL TUMOR OF THE LUNG

Cell Type	Histiocytes	Squamous Carcinoma	Giant Cell Tumor
General Criteria	Usually single	Single or in group with molding and structural formation (pearls)	Usually single
	Fairly constant shape (oval)	Marked variation in shape	Moderate variation in shape (round or oval)
	Fairly constant in size	Variable in size	Marked variation in size
	Possible mitosis	Rare mitosis	Frequent mitosis
Cytoplasm	Sharp borders	Sharp borders	Rather indistinct borders
	Adequate	Variable	Usually scanty
	Basophilic vesicular with ingested debris in vacuoles and carbon particles	Eosinophilic, thick, hyaline with keratohyaline granules	Eosinophilic and slightly vesicular
Nuclei	Eccentric, round or bean shape touching the cytoplasmic membrane	Variable in shape and position	Tendency to be round and central
	Granular chromatin pattern	Marked hyperchromatism and kariopyknosis	Marked hyperchromatism with irregular chromatin clumping and sharp projections
	Possible multinucleation but with "Mirror like image nuclei"	Usually mononucleated	Frequent multinucleation with difference in size and shape of nuclei

tion in their size and shape. No specific orientation or attempt of differentiation is seen, giving the observer the impression that they could have originated from elsewhere and were collected in the alveolar chambers after their exfoliation. But, if this were true, we should see some degree of degeneration of the cells and the presence of a primary cancer in the bronchial tree. Multiple sections of the lung failed to show a definite area of transition in the bronchial mucosa.

The characteristics of the exfoliated cells seen in the sputa and bronchial washings can be summarized as follows:

General Criteria: The cells are abundant, generally well preserved often in mitosis with a tendency to be round in shape, usually single or in groups of two or three, but with no molding of their structures. The most striking criteria are their marked difference in size and lack of coherence with one another. The cells are independent and have no tendency to form any definite structures.

Cytoplasm: The cytoplasm is generally scanty, eosinophilic and vesicular with indistinct and rather hazy cellular borders. No vacuoles, keratohyaline granules or carbon particles are seen. Few of them showed dark staining cellular debris indicative of some degree of phagocitic capacities.

Nuclei: The nucleus is generally situated in the center, not touching the cytoplasmic border, usually multiple, with marked hyperchromasia and marked variations of their size and shape. The nuclear membrane is sharp with marked irregularity of its thickness. The chromatin is abundant, in clumps, with irregular pointed projections and indentations. In considering the differential diagnosis of these cells, the active histiocytes, as seen in the expectoriated materials of patients with acute pulmonary pneumonitis, abscess or infarct, are the worst ones to differentiate. A summary of differential criteria between the exfoliated cells of a giant cell tumor, a bronchogenic squamous carcinomas, and active inflammatory histocytes is given in the previous table.

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Herpes Zoster Pneumonitis: Case Report

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Herpes zoster is well known for its cutaneous manifestations, but reports of its visceral involvement are infrequent in medical literature. This may be due to the actual rarity of the condition; however, the number of cases in some reports[1,2,5] suggests that the frequency may be related to the intensity of investigation of complications of this ordinarily mild disease. It is likely that none of the major viscera is immune to involvement in those few cases in which the manifestations are not limited to the skin. Some of the symptoms of the usually transient visceral manifestations may be functional; however, non-specific organic lesions have been demonstrated by endoscopy or surgical exploration in a number of cases.[3-4] Pneumonitis has been demonstrated in only a few of those cases with presumed herpes zoster of the respiratory tract. Pleuritic rubs,[1] bronchitis,[1] tracheitis and laryngitis[2] are reported. Gais and Abrahamson[1] described one case of x-ray film demonstrating pulmonary consolidation in seven cases with abnormal pulmonary and pleuritic physical findings. Andrews[4] quotes Herbeuval[5] *et al.* as reporting three cases of pulmonary consolidation associated with thoracic herpes zoster and then reported one of his own.

Case Report

This well developed, well nourished 35 year-old white man was seen June 12, 1959 because of substernal aching pain on deep inspiration. This complaint had been present for one week. There was no dyspnea or sputum and very little cough. Inventory of systems was negative. He was an oil refinery worker, but there was no history of exposure to noxious agents. Past history was negative except for a brief episode of uncomplicated pleurisy in 1944.

On physical examination, he appeared well. There was no cyanosis or dyspnea. Temperature was 100°F. Pulse was 96 per minute. Respiration was 16 per minute. A large zone of herpes zoster was noted involving the anterior, lateral and posterior distribution of the left fourth and fifth intercostal nerves. The lungs were entirely clear to physical examination.

The erythrocyte sedimentation rate was 51 millimeters in one hour. The white blood count was 9.2 thousand (73 per cent segmented polymorphonuclear leukocytes, 25 per cent lymphocytes and 2 per cent eosinophils). Red blood cell count was 4.53 million. Hemoglobin was 14.3 grams. Kahn was negative.

FIGURE 1

FIGURE 2

A chest x-ray film (Figure 1) on June 12, 1959 showed two medium sized patches of centrally located soft infiltration in the left mid and lower field, possible left hilar lymphadenopathy and fuzzy appearance of the central portion of the right leaf of the diaphragm.

Symptomatic treatment was instituted and clinically the case was that of an uncomplicated herpes zoster. The skin lesions were completely clear by July 6, 1959 and the chest x-ray film on that date (Figure 2) was "normal" except for suggestion of persistence of the left hilar adenopathy. Chest x-ray film on October 10, 1959 was entirely normal as compared to a routine film made a year prior to the episode of herpes zoster.

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MUSCLE DEFECT PLASTY FOLLOWING ESOPHAGOMYOTOMY

Experimental data concerning the use of the omentum after esophagomyotomy are presented. Twelve dogs have been taken for the study.

In a series of experiments in 12 dogs, esophagomyotomy was followed by closing the muscle defect of the esophagus with an omental pedicled graft. In control series such plastic procedure was not applied. It was found that the omentum is not subject to scarring and prevents the formation of scars about the esophagus.

In case of mucosal injury, the omentum prevents suppurative complications.

Vasiljev, V. N., and Zukerman, I. Y.: "Muscle Defect Plasty following Esophagomyotomy," *Surgical Review (USSR)*, 86:16, 1961.

MANAGEMENT OF DISSECTING ANEURYSMS OF THE AORTA

Early operation on patients with ascending aortic tears is not advised unless the patient is young and has a healthy myocardium. This would probably occur only in Marfan's syndrome. For dissections which start at or beyond the left subclavian artery, it is possible to resect the segment bearing the intimal tear and to close the false channel distally. In spite of the hazards imposed by advanced disease of the aortic wall, attempts to save life in such acute dissections with a known high mortality seem entirely justified.

Two adjuncts are essential to the planning and execution of appropriate surgical treatment. The first is radiographic delineation of the location and extent of disease by venous angioaortography, and the second is utilization of atrio-femoral by-pass during the period of aortic occlusion.

Lyons, C., and Simpson, W. F.: "An Outline of Management of Dissecting Aneurysms of the Aorta," *J. Med. Assoc. Alabama*, 30:469, 1961.

Rupture of Bronchus with Recurrent Stricture Following Primary Anastomosis

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In April, 1959, at the annual meeting of the American Association for Thoracic Surgery, Hood and Sloan presented an analysis of all cases of injuries of the trachea and major bronchi since the review by Kinsella in 1947. They noted that pulmonary resection had been utilized far too often in recent years and emphasized that repair of such injuries without sacrifice of lung tissue is feasible in the majority of cases. They presented seven cases in their own series, including one that had plastic repair of a recurrent stricture.

This is a case report of recurrent stricture following primary anastomosis and for which dermal grafting was subsequently utilized with an apparent successful result. It is being presented in detail because of some unusual aspects of the problem and some observations that might be useful in the diagnosis and management of similar problems.

This 28 year-old white woman was seen in consultation at the Dearborn Hospital in Madera, California on February 25, 1958, approximately 24 hours after she was injured in an automobile accident. X-ray films on February 24 had revealed considerable emphysema with a suggestion of partial collapse of the left lung by pneumothorax, but the lung fields appeared essentially clear. Other injuries included fractures of the mandible, right femur, left clavicle, and left scapula. She was placed in traction in an oxygen tent and given three units of blood in the next 24 hours. A repeat portable chest film on February 25 (Figure 1) revealed increased pneumothorax on the left. There was generalized haziness throughout the right lung, suggesting diminished aeration and patchy areas which were interpreted as atelectasis, pneumonitis or hemorrhage into the lung parenchyma.

Physical examination revealed a well-developed and nourished white woman in an oxygen tent, appearing drowsy from recent medication, but responding to stimulation. Her pulse was rapid but regular. There was no cyanosis. Respirations were regular, about 24/minute, but quite noisy as though she had retained secretions. There was considerable subcutaneous emphysema over the chest and neck, extending up to the scalp. Breath sounds were absent on the left and coarse rhonchi were heard on the right.

She was prepared for tracheostomy and left thoracostomy with tube drainage. It was planned to do these procedures under local anesthesia, but, on removal from the oxygen tent, she became apprehensive, restless and dyspneic. A catheter was passed blindly into the trachea, and the aspiration of a moderate amount of bloody secretion resulted in some improvement. A general anesthetic was then administered and an endotracheal tube was inserted. The anesthetist remarked that there appeared to be resistance to his bag pressure throughout the operative procedure. A large Foley catheter was inserted in the left second anterior interspace with evacuation of a large amount of air. A No. 6 tracheotomy tube was inserted with aspiration of a moderate amount of bloody secretion. However, she continued to have a wheezing type of respiration and diminished air exchange, even though breath sounds were heard bilaterally. Rapid, labored respirations continued on return to the ward, and her condition was considered critical.

During the next few days she showed gradual general improvement, but bilateral wheezing persisted. An x-ray film on February 28, 1958, revealed good aeration of both lungs, although breath sounds were diminished on the right side. On March 4 there was still considerable wheezing bilaterally, but on March 7, breath sounds were entirely absent on the right side and the left lung was clear. An x-ray film on March 8 (Figure 2) still revealed good aeration of both lungs. Part of one tooth was missing and foreign body in the right main-stem bronchus was considered a possibility.

On March 11, 1958, a 5 mm. bronchoscope was inserted through the tracheostomy and the right main-stem bronchus was found to be blocked by granulation tissue at the level of the carina. Breath sounds were not noted following partial removal of the granulations with the foreign-body forceps. Rupture of the bronchus was suspected for the first time on this examination, and the findings at repeat bronchoscopy on March 18 seemed fairly conclusive. This time a 7 mm. bronchoscope was used, and the right main-stem bronchus was again noted to be partially occluded by granulation

tissue a short distance below the carina. After removing some of the granulations, a 5 mm. bronchoscope could be passed beyond the obstruction, but the usual landmarks could not be identified. Faint breath sounds were heard afterwards, but an x-ray film on March 19 (Figure 3), revealed the right lung completely opaque with the trachea deviated to the right. It was obvious that the right main-stem bronchus had been ruptured at the time of the accident, and the right lung was now functionless.

It was felt that some attempt at plastic repair should be made, but in the presence of the other multiple injuries, it was difficult to decide just when surgery should be performed. Consultation regarding the fractured jaw and severe fracture of the femur indicated that the pulmonary problem took precedence. Meanwhile a repeat bronchoscopy on April 3 revealed complete occlusion of the right main-stem bronchus by fibrostenosis just below the level of the carina.

Right thoracotomy was performed on April 9, 1958, 44 days following injury, and the right lung was found to be completely atelectatic. Scar tissue in the region of the right main-stem bronchus made dissection tedious, but it was soon apparent that there had been complete transection of the bronchus at the carina, with the distal end retracted about 1½ cm. and a thick fibrous band between the stumps. Reimplantation of the right main-stem bronchus into the trachea was considered the procedure of choice. The distal stump was incised and viscid mucoid secretion was aspirated. An asepto syringe and rubber catheter were used to partially inflate the lung, and all lobes expanded. The end of the bronchus was trimmed for anastamosis, and it was noted that the transection was just proximal to the upper lobe orifice with no encroachment on the lumen of this orifice. A window was made in the trachea near the carina, and the anastamosis was made with interrupted sutures of tantalum wire. A free pericardial fat-pad graft was used to cover the suture line anteriorly. At the time the trachea was opened, the endotracheal tube was passed into the left main-stem bronchus. On enlarging the tracheal opening, the cuff on the tube was nicked and deflated, but the tube still fit snugly in the left bronchus. However, on withdrawing the tube into the trachea to inflate the right lung, the control of the patient's respirations was not too good. The chest was closed quickly and the condition improved. At conclusion of surgery, the tracheotomy tube was replaced. Good breath sounds were heard bilaterally.

The immediate post-operative course was uneventful and x-ray films on April 11, and April 17, 1958 showed the right lung well aerated. Breath sounds were absent from about the eighth post-operative day, however, and bronchoscopy on April 24 revealed partial occlusion of the anastamosis by granulation tissue. After removing some of the granulations with the suction tip, it was possible to pass the 5 mm. bronchoscope. The bronchus beyond appeared normal except it was impossible to identify the upper lobe orifice. The wire sutures were not visible. In spite of repeat bronchoscopies with dilatation, stenosis was progressive and on June 13 it was impossible to pass even the smallest bougie. It is interesting that all x-ray films showed the right lung well expanded (Figure 4) in spite of the marked stenosis and absence of breath sounds.

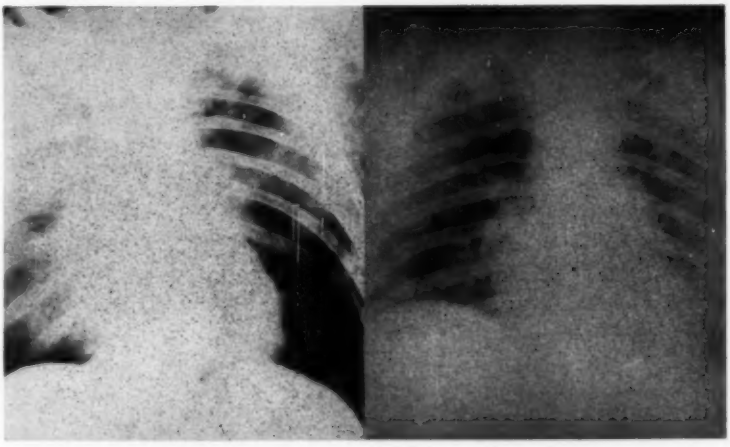


FIGURE 1 FIGURE 2

FIGURE 1: X-ray film 24 hours after injury showing left pneumothorax and subcutaneous emphysema. FIGURE 2: X-ray film 12 days after injury showing good aeration of both lungs although breath sounds were absent on the right side.

Repeat thoracotomy was performed on July 2, 1958, and the lung was still aerated. There was dense scar tissue over the anastomosis and the pulmonary artery. The bronchus was dissected free and an incision was made in the membranous wall near the upper lobe bronchus extending through the stenotic area a short distance on to the trachea. The edges separated about 1 cm. and the incision measured about one and one half cm. A full-thickness dermal graft was taken from the lower part of the incision, denuded of its epidermis, and reinforced with No. 30 stainless steel wire. It was sutured in place with 4-0 chronic catgut. The lung inflated readily. The postoperative course was uneventful, and she was transferred to the Fresno County Hospital on July 14, 1958, for further care.

Bronchoscopy on July 23, 1958 revealed a small amount of granulation tissue at the site of anastomosis, and this was cauterized with 20 per cent silver nitrate. The main-stem bronchus appeared collapsed at this level, but admitted easily bougies up through No. 22. Subsequent bronchoscopies were performed at intervals of about three weeks, and dilatations were necessary until December 2, 1958. A wire suture was removed on one occasion and this was thought to be the one used to reinforce the dermal graft. Iodized oil (Lipiodol) was instilled on February 11, 1959 (Figure 5) with excellent filling of all lobes and no evidence of bronchiectasis. At bronchoscopy on September 16, 1959, the 7 mm. bronchoscope was easily passed into the right main-stem bronchus.

Now she is in good general condition 23 months after the injury and 18 months after the second bronchoplasty. Breath sounds are excellent on the right side, and there is no indication of diminished respiratory reserve. The tracheostomy was kept open by tube and later by plastic plug to facilitate bronchoscopies. The plug was removed in May, 1959, and the wound healed within four weeks. She has been able to resume activities which includes singing as a part-time entertainer.

Discussion

In retrospect it would appear that the diagnosis should have been established earlier. Initially attention was focused on the left chest because of the obvious pneumothorax. Nevertheless, there were other signs which should have at least suggested rupture of the bronchus as a possibility. The anesthetist observed, at the time of initial intubation, that there was resistance to bag pressure even after the pneumothorax had been relieved and a good airway established. Also wheezing respirations persisted on the right side after suctioning of the tracheobronchial tree through the tracheotomy tube. Foreign-body in the bronchus (aspiration of tooth) was considered as a possible explanation for the wheeze, and in retrospect this was not likely in the absence of x-ray evidence of an opaque foreign-body.

Bronchial rupture was not seriously entertained as a possibility until the bronchoscopy on March 11, 1958, 14 days after the initial injury. Earlier diagnosis would not have altered the treatment, since the other injuries were of such magnitude that no major procedure would have been contemplated as long as the patient's condition

FIGURE 3

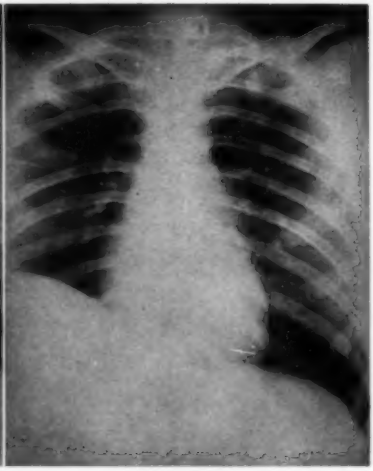
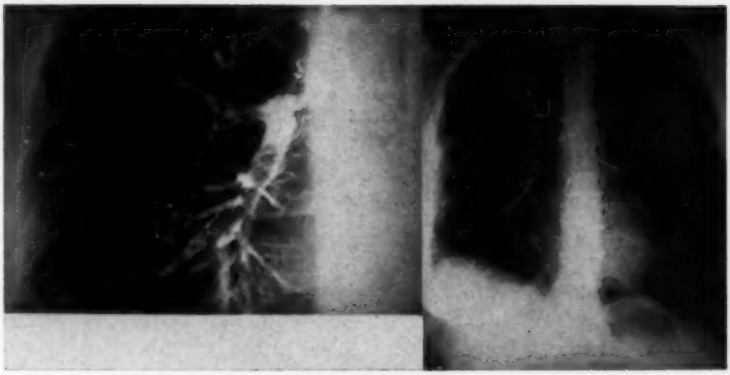


FIGURE 4

FIGURE 3: X-ray film 23 days after injury showing complete atelectasis of right lung. **FIGURE 4:** X-ray film three months following primary anastomosis. Restenosis has occurred.



FIGURES 5

FIGURE 5: (two films). Bronchogram two months after dermal grafting revealing right main bronchus widely patent and no evidence of bronchiectasis.

was stabilizing. However, it would seem in this case that to consider the possibility of bronchial rupture would be to make the diagnosis.

Tracheostomy facilitated the subsequent management of the problem. She tolerated the tube and later the plastic plug so well that the tracheostomy was maintained throughout the entire 15 months of treatment. She was apprehensive and would not have permitted bronchoscopy by the oral route with the usual topical anesthesia. Light general anesthesia was usually given, but bronchoscopy was accomplished easily and was used freely. It is interesting that the tracheostomy wound closed spontaneously within four weeks after removal of the tube.

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TUBERCULOUS MENINGITIS

A group of 50 children who recovered from tuberculous meningitis on treatment with SM and INH have suffered a significant degree of intellectual impairment. It appears that the factor having the most unfavorable influence in intellectual recovery is severe clinical illness as evidenced by convulsive seizures.

Loss of consciousness for some time during the early phase of tuberculous meningitis in itself does not appear to be a highly unfavorable sign. Nevertheless, when unconsciousness is associated with convulsive seizures, the intellectual functioning of the patient, in most instances, can be expected to be seriously impaired.

An infant with tuberculous meningitis may be expected to have an unfavorable prognosis aside from any other factors. An older child who has remained conscious throughout his illness and without convulsions, may be expected to have a relatively good prognosis.

Nickerson, G., and MacDermot, P. N.: "Psychometric Evaluation and Factors Affecting the Performance of Children Who Have Recovered from Tuberculous Meningitis," *Pediatrics*, 27:68, 1961.

X-RAY FILM OF THE MONTH

Edited by Benjamin Felson, M.D.

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Clinical History

A 58 year-old white man was first seen in the University of Oklahoma outpatient clinic in 1954 complaining of weight loss, chest pain and dyspnea. A chest x-ray film (Fig. 1) demonstrated a small left pleural effusion and questionable hilar lymphadenopathy. Granulomatous infiltration and sarcoidosis were considered clinically. All skin tests were negative.

He left the state and was not seen again until 1958, when congestive heart failure was thought to be present. Multiple systemic complaints were present. Chest roentgenograms (Fig. 2) revealed several spherical densities in the parenchyma resembling metastatic disease. Thoracic laminograms were compatible with metastatic nodules, although granulomas could not be excluded.

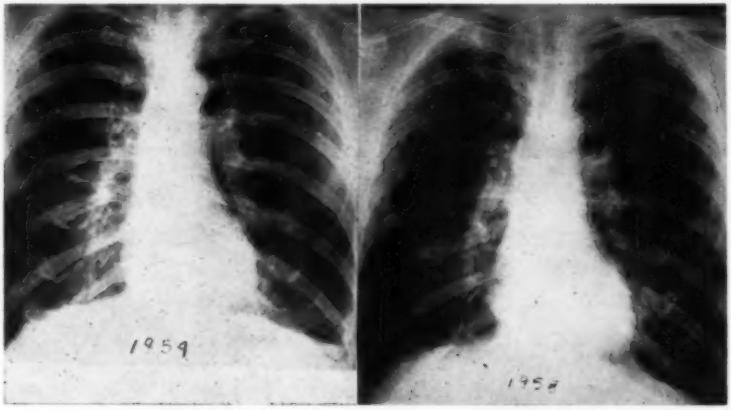

FIGURE 1: Postero-anterior chest film, 1954.

FIGURE 2: Postero-anterior chest film, 1958.

An intensive search of the gastrointestinal tract, nasopharynx and paranasal sinuses failed to identify a primary site. Films of the extremities showed rheumatoid changes in the phalanges. Skull films were negative.

In January, 1959, thoracotomy was performed and a lung biopsy was reported to show caseating chronic granuloma. The patient was discharged with the diagnoses of chronic pulmonary granulomatous disease and rheumatoid arthritis.

The patient was readmitted in August, 1960, with evidence of pulmonary decompensation, malaise, emaciation and bizarre neurologic

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findings suggesting lower motor neuron involvement. Ischemic changes in the phalanges bordered on frank gangrene. A chest x-ray film (Fig. 3) revealed extensive bilateral fibrotic and nodular infiltrate, pleural effusions, and evidence of generalized loss of lung volume.

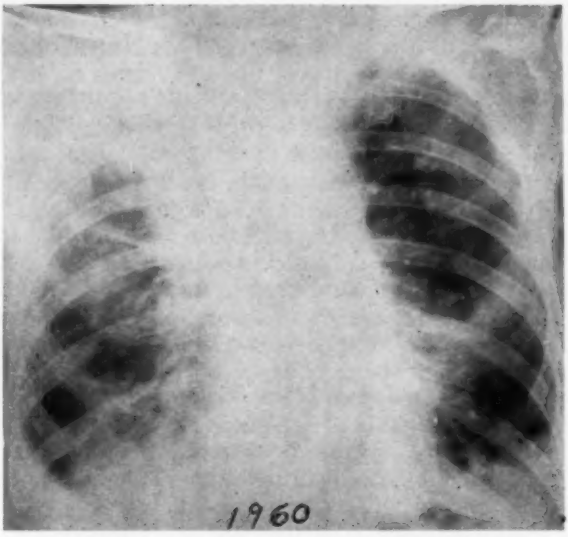

FIGURE 3: Postero-anterior chest film, 1960.

Answer: WEGENER'S GRANULOMATOSIS

The Department of Radiology suggested the diagnosis of Wegener's granulomatosis on the basis of the roentgen appearance of the lungs, biopsy material and the presumptive presence of arterial disease. Biopsies were obtained of the deltoid muscle and an axillary lymph node. The pathologic report was chronic lymphadenitis and periartertitis nodosa. These findings were felt to be compatible with Wegener's granulomatosis. A genito-urinary work-up was negative.

The patient was begun on large doses of steroids and general supportive measures with some subjective clinical improvement.

The Committee on Chest Roentgenology welcomes comments. We would also be pleased to receive x-ray films of exceptional interest with brief history. Please submit material to: Benjamin Felson, M.D., chairman, Department of Radiology, Cincinnati General Hospital, Cincinnati, Ohio.

SECTION ON CARDIOVASCULAR DISEASES

Pericardial Effusion in Congestive Heart Failure*,**

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HERBERT M. STAUFFER, M.D., and LOUIS A. SOLOFF, M.D.
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Enlargement of the cardiac silhouette is a cardinal finding in congestive heart failure. This enlargement is attributed to dilatation of the cardiac chambers which have failed. Abnormally large accumulations of extravascular fluid are also cardinal signs of congestive heart failure. Such fluid may be present beneath the skin, in the peritoneal cavity and in both pleural cavities. Necropsy may disclose a variable increase in pericardial fluid in the presence of cardiac failure. The enlarging cardiac silhouette which develops during congestive failure therefore may be due to both cardiac dilatation and pericardial effusion. Conventional methods of study, including clinical, electrocardiographic and roentgenologic examinations, are not capable of differentiating the role that each of these two may play in contributing to such enlargement. Angiocardiography is a definitive method of detecting the presence and frequently the amount of pericardial effusion whether the enclosed cardiac silhouette is normal in size or is enlarged.[1] This technique does not appear suitable, however, for routine comparative diagnostic studies because of the amount of roentgen ray exposure, the need for an incision and the need for special apparatus. The demonstration that intravenous carbon dioxide is a safe method of visualizing right atrial pericardial thickness suggests the use of this procedure as a simple diagnostic test to determine the presence of pericardial effusion when congestive heart failure is present.[2]

Material and Methods

Eighteen subjects, ten men and eight women, 37 to 74 years of age, were studied. Seven had rheumatic, six coronary and four hypertensive heart disease. One had heart disease of unknown cause. The only basis for selection of subjects for study was the presence of peripheral signs of congestive heart failure. All were weighed on admission into the hospital and had routine laboratory studies including an electrocardiogram and a roentgenogram of the chest.

Carbon dioxide (USP) was used for the gas angiocardiogram. It is important to note that this gas differs from the usual mixture of carbon dioxide and oxygen in hospital practice. The subject lies in the left lateral decubitus position. A 19 or 20 gauge needle is inserted into the left median

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antecubital vein. The needle is connected to an intravenous drip through a 3-way stopcock so that the needle can be kept open in the intervals between gas injections. A 100 cc. syringe with another three-way stopcock is thoroughly flushed several times with pure carbon dioxide. Then 100 cc. of the gas is injected rapidly into the vein. Originally, an exposure was made at the end of the injection, and a second exposure was made within a few seconds thereafter. The films were checked while wet after processing, and a second injection was made if indicated.

This technique was used because of our desire for a simple, readily available method of detecting pericardial effusion. In general, this technique is staisfactory, although on occasion difficulties in interpretation may arise. More recently cineradiography has replaced our film technique. A 16 mm. camera taking 64 frames a second is utilized. Details of the study of the right atrial pericardial wall are increased by re-playing the film at 16 frames a second.

Such studies were carried out on each subject on admission into the hospital and were repeated after maximal benefit was obtained with appropriate therapy. At this time, all subjects were re-weighed and all received an electrocardiogram and a chest roentgenogram.

A diagnosis of pericardial effusion was made if the right atrial pericardial wall at its narrowest was more than 4 mm. in diameter.

Results

Six of the 18 subjects had definite evidence of pericardial effusion. Characteristic findings are shown in Figures 1 and 2. Four of these six had rheumatic heart disease, one had hypertension and one coronary artery disease who, in addition, was thought to have a collagen type of disease resembling rheumatoid arthritis. Two of these six subsequently died. Both had rheumatic heart disease and pericardial effusion was found at necropsy.

The one with heart disease of unknown cause had questionable evidence of pericardial effusion. Although the right atrial pericardial wall was apparently 5 mm. thick, it could not be distinctly separated from

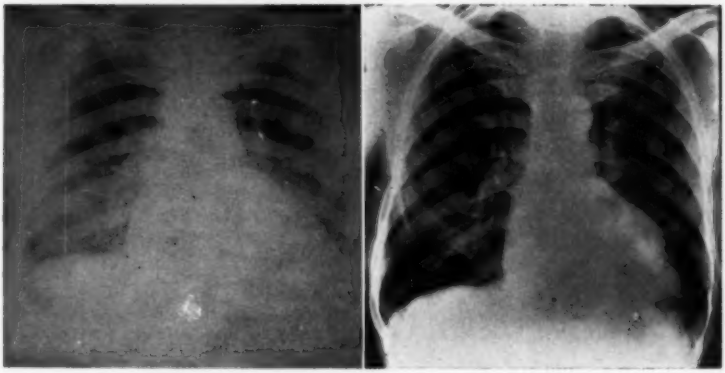

FIGURE 1A FIGURE 1B

FIGURE 1: P.B., 61 year-old man. (A) Taken during congestive heart failure; (B) After dissipation of failure.

pulmonary vascular markings which overlapped part of the right atrial pericardial wall. Two others had inconclusive evidence of pericardial effusion for the same reason. The right atrial pericardial wall was 2 to 4 mm. thick. One of these two subsequently died. No pericardial effusion was found at necropsy.

Five of the 18 subsequently died. Necropsy was performed in four of these five. Two diagnosed as having no pericardial effusion during life had none at necropsy. The diagnosis of effusion during life in one was confirmed by paracentesis and also by necropsy. The last one diagnosed as having pericardial effusion during life died three months after the

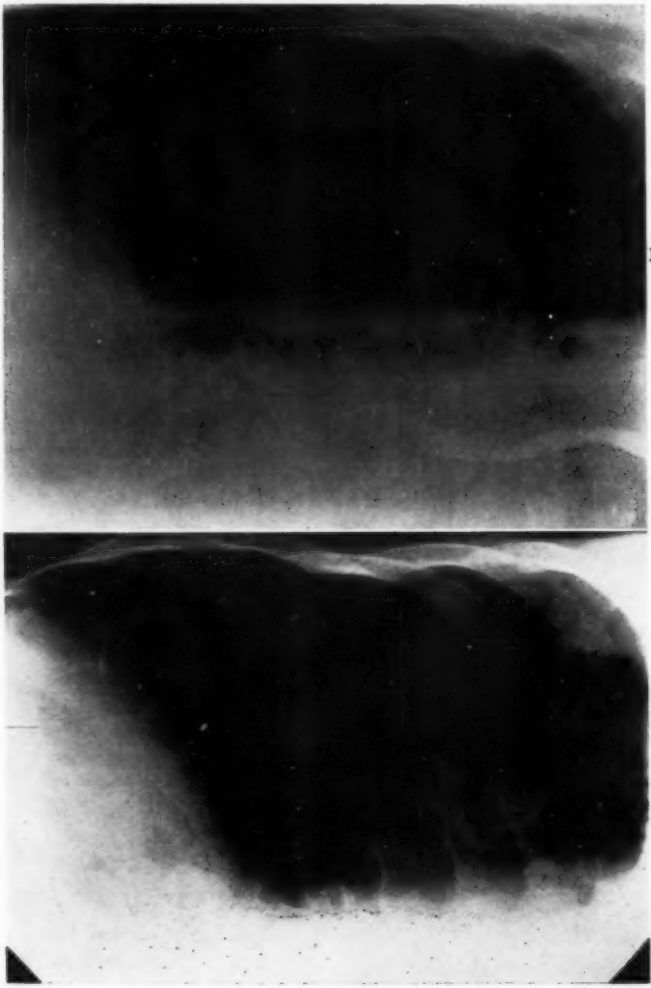

FIGURE 2A

FIGURE 2B

FIGURE 2: Same patient. CO_2 gas angiocardiogram. (A) taken during congestive heart failure; (B) after disappearance of failure; right heart border diameter is 0.2 cm. Note that there is nothing in the conventional film (Fig. 1A) to indicate the presence of pericardial effusion.

initial gas angiocardiogram had been performed. Only 80 cc. was removed from the pericardial cavity. Peripheral signs of congestive heart failure persisted until death, but were considerably less than those present when the carbon dioxide study was performed.

Only one subject with pericardial effusion had a considerable decrease in the size of the cardiac silhouette after restoration of compensation. He had rheumatic heart disease. Otherwise, reduction in the size of the cardiac silhouette occurred with appropriate therapy for cardiac failure regardless of whether or not pericardial effusion was present.

Retrospective studies of conventional chest films failed to disclose features which could separate those with from those without pericardial effusion. Similarly, neither the history nor the clinical findings were of value in differentiating the two groups. There is also no relationship between the amount of effusion and the degree of peripheral signs of congestive heart failure.

Discussion

It was anticipated on theoretical grounds that pericardial effusion would be uncovered in subjects with congestive heart failure if a technique were used which could separate a pericardial reaction with effusion from the enlarged cardiac silhouette. After all, effusions in other serous cavities are a common finding in heart failure. Yet, pericardial effusion was demonstrated in only one-third of our subjects.

It is important to bear in mind that although a diagnosis of pericardial reaction can be made with confidence when the right atrial pericardial border is clearly delineated and thickened, such a diagnosis may be obscured by overlapping pulmonary structures which are frequently accentuated by congestion. A great part of this difficulty may be resolved by employing cineradiography. More important, perhaps, is the fact that this type of study is limited to visualizing the right atrioventricular border in the left lateral recumbent position. It is possible that small accumulations of fluid may gravitate away from this wall. Certainly only a rough index of the quantity of pericardial effusion can be estimated by this means. It is likely therefore that pericardial effusion in some excess in congestive heart failure may be more common than our findings indicate. Nevertheless, it is unlikely that effusion is abnormally large when pericardial effusion is not detected by gas angiocardiogram.

In this small series, treatment was equally effective or ineffective in restoring compensation or in preventing death whether effusion was present or not. As previously stated, the presence or absence of pericardial effusion is not related to the degree of peripheral manifestations. Pericardial effusion in this series, therefore, had no prognostic or therapeutic significance.

It is, however, particularly noteworthy that four of the six with pericardial effusion were found in those with rheumatic heart disease. None of these four had clinical or laboratory evidence of active rheumatic carditis. One of the other two had coronary artery disease and a form of rheumatoid arthritis. In spite of this high incidence of rheumatic heart disease in those exhibiting pericardial effusion, almost two-thirds of our subjects did not have rheumatic heart disease. This incidence strongly suggests that pericardial effusion in congestive heart failure is not due simply to transudation as occurs elsewhere in the body when congestive heart failure is present. The high incidence of rheumatic heart disease suggests, rather, that local pericardial factors such as antecedent or co-existent pericardial disease are the determining factors in the presence of pericardial effusion in congestive heart failure. That the pericardium in contrast to other regions of the body does not constantly have significant accumulations of fluid in the presence of congestive heart failure indicates that the pericardium differs from other serous cavities in its ability to transfer water and electrolytes. Burch and Ray have shown the tremendous power of the dog's pericardium to reabsorb electrolytes injected into its cavity.[3] They stated that this tendency of the test fluid to be reabsorbed is an expression of the normal physiologic factors concerned with maintaining a relatively small volume of fluid in the pericardial cavity. The heart's motion may be an important contributing factor. This function apparently persists in the presence of congestive failure. Local pericardial disturbances may interfere with this function and act as the major cause for accumulation of excessive fluids within it.

SUMMARY

1. Films exposed after intravenous carbon dioxide uncovered pericardial effusion in six of 18 subjects with congestive heart failure.

2. These instances of effusion occurred predominantly in those with diseases which are prone to effect the pericardium.

3. Local pericardial factors are the most likely cause for the presence of significant pericardial effusion in congestive heart failure.

4. Pericardial effusion in congestive heart failure has no prognostic significance.

RESUMEN

1. Las peliculas tomadas despues de inyección intravenosa de Bioxido de carbono permiten descubrir derrames pericárdiacos en seis de 18 enfermos con insuficiencia cardiaca congestiva.

2. Esto casos de derrame ocurrieron predominantemente en afecciones que tienen tendencia a desarrollar derrame pericárdiaco.

3. Los factores locales pericárdiacos son las causas mas probables para la presencia de esos derrames.

4. El derrames pericárdiaco en la insuficiencia cardiaca congestiva no tiene significación pronóstica.

RESUMÉ

1. Des films pratiqués après injection intraveineuse de gaz carbonique mirent en évidence un épanchement péricardique chez six malades parmi 18 atteints d'insuffisance cardiaque.

2. Ces épanchements survinrent d'une façon prédominante chez ceux qui étaient atteints d'une affection qui touche avec prédilection le péricarde.

3. Des facteurs locaux péricardiques sont la cause la plus vraisemblable de la présence d'un épanchement péricardique important lors des atteintes cardiaques.

4. L'épanchement péricardique n'a pas de signification pronostique.

ZUSAMMENFASSUNG

1. Filme, die nach intravenöser CO_2—Verabfolgung exponiert wurden, ergaben einen Herzbeutelerguß bei 6 von 18 Fällen mit Herzdekompensation.

2. Dieses Vorkommen eines Ergusses trat vorwiegend bei solchen Patienten auf, die an Krankheiten litten, die dazu neigen, das Perikard zu befallen.

3. Lokale, mit dem Perikard verknüpfte Faktoren sind sehr wahrscheinlich die Ursache für das Auftreten erheblicherer Herzbeutelergüsse bei Herzdekompensation.

4. Dem Herzbeutel-Erguß kommt bei Herzdekompensation eine prognostische Bedeutung nicht zu.

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RETREATMENT OF TUBERCULOUS PATIENTS

Retreatment of tuberculous patients with the newer antimicrobial agents has been shown to produce gratifying results though it leaves much to be desired. An optimistic view cannot be held for such treatment because the results are so inferior to adequate chemotherapy in the initial cases. Retreatment of established failures with daily streptomycin and high doses of INH, with or without PAS, appears to have some advantage particularly in those whose chemotherapeutic history is of fairly short duration and whose sputum cultures show a persistently positive catalase reaction.

Saliba, A., and Beatty, O. A.: "Retreatment of Tuberculous Patients: An Experience with the Combined Use of High Doses of Isoniazid, Pyrazinamide and Cycloserine," *Southern Med. J.*, 54:10, 1961.

Role of Hypothermia in the Protection of Myocardial Metabolism during Cardiopulmonary By-Pass and Elective Cardiac Arrest*,**

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It is recognized that present-day techniques of intracardiac surgery demand a satisfactory method of elective cardiac arrest. Potassium citrate, acetylcholine and hypoxic arrest have all been used with varying degrees of success. Each of these methods has its limitations and with each, difficulties in resuscitation are encountered. In general, because of the greater ease of resuscitation, hypoxic arrest seems preferable to potassium citrate or acetylcholine. Our previous studies[1] suggest that hypothermia offers some degree of protection to myocardial metabolism by preserving sources of energy for myocardial contraction. It was demonstrated that when the dog's heart was permanently arrested at normothermia with potassium citrate, myocardial glycogen values decreased by 78 per cent, ATP by 60 per cent and lactic acid increased by 500 per cent by the end of 90 minutes of arrest. When animals were placed on cardiopulmonary by-pass and arrest produced with potassium citrate or hypoxia for 30 minutes these changes were of the same order. When total body hypothermia was utilized with by-pass, however, with myocardial temperature reduced below 20°C., glycogen values were essentially unaltered and lactic acid increased to a less degree. Adenosine triphosphate and phosphocreatine values were less consistent, but some degree of protection by hypothermia was suggested. These results are similar to those recently presented by Gott.[2] Cardiac resuscitation after arrest with potassium citrate or hypoxia has been shown to be poor after periods of 20 minutes. When hypothermia was utilized with arrest, resuscitation was accomplished in all cases with ease. Therefore, these biochemical studies correlated well with the observation that the heart behaves better functionally when hypothermia is used. Since the more complicated cardiac defects often necessitate cardiac arrest for prolonged periods of time, it seemed desirable to study further the protection afforded by hypothermia when used with cardiopulmonary by-pass and hypoxic arrest, and to establish the length of time over which this protective effect might be effective.

Methods

Mongrel dogs, weighing 12-15 kg., were placed on cardiopulmonary by-pass with a Kay-Cross disc oxygenator and a DeBakey roller pump. Right thoracotomy was performed through the fourth intercostal space.

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Venous cannulation was through separate openings in the right atrium, #24 and #26 French catheters being used for the superior and inferior vena cavae respectively. Arterial cannulation was through a femoral artery, the largest possible size cannula being inserted. Pressures were monitored via the opposite femoral artery and an upper extremity or cervical vein by transducer connected to a Grass multichannel recorder. A single lead electrocardiogram was continuously recorded. Mid-esophageal temperature was recorded with a Yellow Springs single channel unit and on ocasion, esophageal, rectal, myocardial, hepatic, cerebral, thigh muscle, as well as inflow and outflow blood temperatures, were simultaneously recorded with a Leeds-Northrup unit. The pump head was made approximately occlusive and flows were monitored as previously described.[3] A Ward Laboratories heat exchanger unit was inserted into the arterial inflow line. When the animal's temperature was maintained at a normal level during by-pass, the maximum pump flow that could be obtained was utilized and this was dependent upon venous return. On the other hand, when hypothermia was used, flow was regulated to produce a mean systemic pressure greater than 75 mm.Hg. Sometimes at temperatures in the range of 20°C. or below, pump flow could be reduced to as low as 25 cc. per kg. or less.

In one group of three animals, temperature was maintained at normal levels while hypoxic arrest was produced by simple occlusion of the ascending aorta for 30 minutes. In a second group total body hypothermia was produced by means of the heat exchanger. When mid-esophageal temperature, previously shown to reflect myocardial temperature, reached 20°C. or below, the ascending aorta was occluded for 30 minutes in three dogs, 60 minutes in four, 90 minutes in two, 120 minutes in two, and four and one half hours in one. Myocardial biopsies were taken from the left ventricle (1) prior to going on by-pass at normal temperature, (2) after temperature had been reduced below 20°C. and just prior to

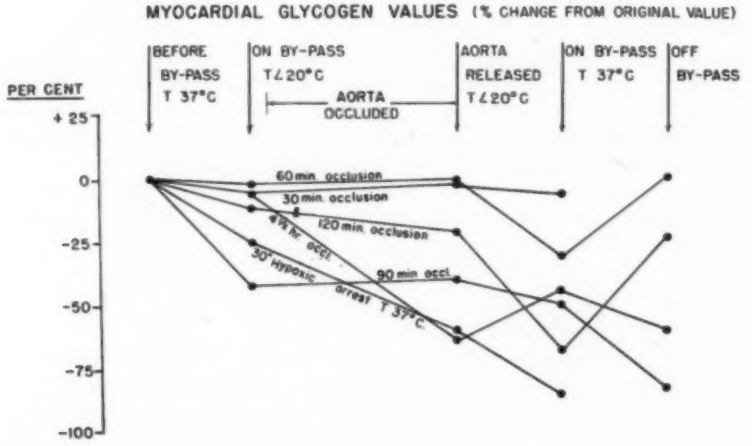

FIGURE 1: Chart comparing changes in myocardial glycogen during 30 minutes hypoxic arrest at 37°C. with those at 30 minutes, 60 minutes, 90 minutes, 120 minutes and four and one half hours at 20°C.

aortic occlusion, (3) just prior to release of aortic occlusion, (4) approximately 30 minutes later when temperature had been returned to normal and the heart resuscitated and (5) another 30 minutes later after by-pass had been discontinued and blood pressure was essentially normal. Biopsies were immediately quick frozen in dry ice and ether and analyzed for glycogen as described by Good, Kramer and Somogyi,[4] lactic acid by the method of Barker and Summerson,[5] adenosine triphosphate and phosphocreatine by technique described by Fiske and Subbarow.[6]

Results

In general, some degree of protection against alterations in normal myocardial metabolism were noted even in the heart arrested for four and one half hours. The degree of protection at one hour was thought to be as good as previously noted in the hearts arrested for 30 minutes (Fig. 1). This was evidenced by the fact that in the 60 minute dogs, glycogen remained at normal and constant level, suggesting that glycogen demands were being met by blood and liver resources. On the other hand, in the hearts arrested for two hours, glycogen values decreased to 20 per cent of the control value by the end of the arrest period. In addition, after restoration of coronary flow with resuscitation to an effective heart beat and normal temperature, glycogen usually continued to decrease but was returning toward normal values some 30 minutes later when off by-pass. In one animal arrested for an hour, glycogen had returned to normal when the last biopsy was taken.

Lactic acid levels increased only slightly in those hearts arrested for 30 minutes and thereafter further increased to about the same degree as the 30 minute hypoxic arrest dog at normothermia except in the dog with four and one half hours arrest (Fig. 2). Lactic acid levels promptly

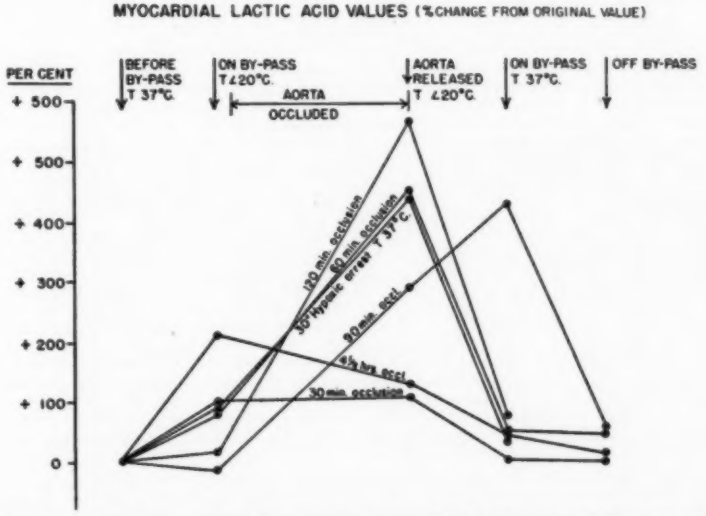

FIGURE 2: Chart comparing changes in myocardial lactic acid during 30 minutes hypoxic arrest at 37°C. with those at 30 minutes, 60 minutes, 90 minutes, 120 minutes and four and one half hours at 20°C.

returned to normal after cardiac resuscitation. This had been observed previously in normothermic hearts arrested by hypoxia or potassium citrate, and suggested that the excess lactic acid is either washed out rapidly with restoration of coronary flow or is utilized as a source of energy. Since a deficit of glycogen exists at this time, lactic acid possibly is metabolized as a source of energy. The low glycogen levels after cardiac resuscitation were noted also previously in hearts arrested by hypoxia or potassium citrate at normothermia. Glycogen deficit was not as great after one hour of arrest with hypothermia as after 30 minutes of arrest at normothermia. In the latter cases, the last biopsy was taken about 20 minutes after cardiac resuscitation and the glycogen levels thereafter are unknown. In the current study with hypothermia, the last samples were taken at least an hour after resuscitation and, in the hearts arrested for one and two hours, these values were increasing toward normal. In the hearts arrested for one and one half and four and one half hours, glycogen values remained low. This deficit in glycogen could be due to its excess utilization or possibly to depletion of liver glycogen, or the hepatic glycogen might be unavailable because of decreased function associated with hypothermia.

Apparently, hypothermia protects against the disappearance of ATP since a higher level was maintained than in the normothermic animals with 30 minutes of hypoxic arrest with the one exception of the four and one half hour dog. In this animal, ATP continued to decrease after resuscitation and increased slightly after by-pass was discontinued, the glycogen curve taking a similar form. The initial glycogen in this animal was about half that of the other animals and it is possible that a poor nutritional status with depleted liver reserve contributed to the delay in regeneration of myocardial glycogen.

Discussion

Evaluation of techniques of producing a quiet, still heart has been carried out by a variety of methods. Wesolowski and associates[7] reported a recovery rate of only 21 per cent after 30 to 60 minutes of myocardial ischemia at normal temperature. This is consistent with observations by others and us that in the experimental animal the incidence of cardiac resuscitation after 20 minutes of hypoxic arrest is quite low. Helmsworth and associates,[8] noted pathological changes in form of focal hemorrhages and fatty degeneration after hypoxic arrest and focal necrosis after potassium citrate arrest. Extensive necrosis after hypoxic arrest has been noted clinically by Lillehei[9] and probably has occurred more often than generally recognized. Other studies have included comparative survival rates between animals undergoing cardiac arrest by various means and those in which the heart was permitted to beat with uninterrupted coronary flow. Recently, studies of ventricular function have been reported upon hearts arrested by various means. Weirich and associates[10] noted that increasing the arrest period from 5 to 20 minutes led to marked impairment in myocardial function with progressive deterioration. The impairment in function was essentially the same for potassium citrate, acetylcholine or simple hypoxic arrest with aortic occlusion. Cooper and associates,[11,12] noted a marked depression of left ventricular function after 30 minutes' arrest with potassium citrate, acetylcholine, a mixture of prostigmine, magnesium sulphate and potassium citrate or hypoxic arrest with aortic occlusion. They noted that the dog's heart arrested with potassium citrate at 28°C. was able to perform approximately twice the stroke of work of hearts arrested at normal temperature. They felt that hypothermia at this level partially protected myocardial function.

Kusunoki and associates[13] studied right and left ventricular stroke work under conditions of arrest with hypoxia, potassium citrate and acetylcholine and found that after 15 minutes of arrest by any of these methods, myocardial function was depressed to 50 to 70 per cent of control function as measured 15 minutes post arrest. Myocardial function was most impaired after hypoxic arrest. Hypothermia to 25°C. partially protected the heart rendered hypoxic for 15 minutes and by this method, there was

least impairment in myocardial function and best recovery after restoration of heart beat. Greenberg and associates[14] also demonstrated that ventricular function after hypothermic asystole was superior to that after other methods of arrest.

Shumway and associates[15] produced regional myocardial hypothermia by dripping cold saline directly upon the heart during cardiopulmonary by-pass until myocardial temperature reached 12°C. The two groups of five dogs each, submitted to 30 and 45 minutes of cardiac anoxia, were all long-term survivors, and four of five dogs survived after 60 minutes of cardiac anoxia.

These observations correlate well with the biochemical studies, indicating the protective influence of hypothermia upon myocardial function. The biochemical studies indicate the manner in which this protective role comes about. While biochemical data indicate only partial protection beyond one hour, some protection was afforded for four and one half hours, evidenced by the fact that this heart easily resuscitated. Ventricular fibrillation developed in all hearts in which hypothermia was used. Usually by-pass was begun with cold blood and ventricular fibrillation usually ensued soon thereafter. This has been our clinical experience also, with ventricular fibrillation usually developing as the temperature reaches the range of 30-32°C. Our early experience indicated that decompression of the left side of the heart was necessary in order to obtain cardiac resuscitation when hypothermia was used.

The continued fall in myocardial glycogen level after restoration of coronary flow and cardiac resuscitation possibly is related to hypothermic effects upon the liver, whose function possibly is impaired for several hours after subjection to hypothermia of this degree. Utilization of selective hypothermia by means of coronary perfusion with cold blood, as has been done clinically by Gott,[16] or by dripping of cold saline directly upon the heart with maintenance of normal body temperature, may have an advantage from this standpoint. In Gott's clinical studies with normal body temperature and perfusion of the heart with cold blood, essentially no alterations in myocardial metabolism were noted during the period of arrest studied. Braunwald and associates[17] have shown that impairment in myocardial function after 30 minutes of hypoxic arrest could be prevented by intermittent release of aortic occlusion. Since oxygen lack during the period of arrest seems to be the critical factor, maintenance of normal temperatures with hypoxic arrest and intermittent aortic release or perfusion of coronaries with cold blood may cause less disturbance in myocardial metabolism.

The results presented are not considered statistically significant, but trends noted seem to justify the stated conclusions. In this study, the values for glycogen, lactic acid and ATP varied widely from one dog to another, possibly related to the fact that many dogs were brought in directly from the streets and used within a day or so. Such experiments probably would be more meaningful if the general status of carbohydrate metabolism of the cntire body were known. Thus, a knowledge of the status of liver glycogen might be helpful in interpretation of the data. Improvement in the nutritional status of dogs preoperatively might enhance the availability of glycogen during the resuscitative period.

While all hearts in this study resuscitated easily and maintained a reasonably normal blood pressure 30 to 60 minutes after resuscitation, bleeding from the site of biopsy usually was extensive and not consistent with long-term survival.

SUMMARY

Appraisal of the biochemical effects of hypoxia upon myocardium during cardiopulmonary by-pass and hypoxic arrest with and without hypothermia has been presented. Metabolic processes were less altered after one hour of hypoxic arrest when hypothermia was used than after 30 minutes at normothermia. Progressive decrease in this protection occurred with passage of time, but some degree of protection was demonstrated after a four and one half hour period of arrest. The correlation between these biochemical findings and observations of myocardial function has been presented. It is suggested that less impairment in myocardial function after hypoxic arrest may result from maintaining a normal body temperature with selective myocardial hypothermia.

RESUMEN

La estimación de los efectos bioquímicos de la hipoxia sobre el miocardio durante la desviación de la circulación cardiopulmonar y la detención hipóxica con o sin hipotermia son motivo de este articulo. Los procesos metabólicos se mostraron menos alterados despues de una hora de paro hipóxico cuando se usó la hipotermia que cuando hubo 30 minutos de normotermia. El decrecimiento progresivo de esta protección occurió al transcurrir el tiempo pero cierto grado de protección, se demostró despues de un periodo de paro de cuatro horas y media. La correlación entre estos hallazgos bioquímicos y las observaciones de la función miocárdiaca se han presentado. Se sugiere que puede resultar daño de la función miocárdiaca despues de paro hipóxico manteniendo una temperatura normal del cuerro con una hipotermia miocárdica selectiva.

RESUMÉ

L'auteur montre l'existence des effets biochimiques de l'hypoxémie sur le myocarde au cours de la circulation extracorporelle et de l'arrêt hypoxique avec et sans hypothermie. Les processus métaboliques furent moins altérés après une heure d'arrêt hypoxique quand on utilisait l'hypothermie qu'après 30 minutes sous température normale. Une diminution progressive de cette protection survint en fonction du temps écoulé, mais un certain degré de protection fut enregistré après une période d'arrêt de quatre heures et demies. Le rapport entre ces constatations biochimiques et les études de lo fonction myocardique sont exposées. L'auteur suggère qu'un trouble moins important de la fonction myocardique après arrêt hypoxique pourrait être obtenu en maintenant le corps à température normale, avec hypothermie myocardique sélective.

ZUSAMMENFASSUNG

Es wird berichtet über eine Bewertung der biochemischen Einwirkungen der Hypoxämie auf das Myocard im Verlauf eines cardiopulmonalen Kurzschlusses und hypoxämischen Stillstandes mit und ohne Unterkühlung. Die Stoffwechsel-Vorgänge waren wenig verändert nach 1 Stunde eines hypoxämischen Stillstandes, falls die Unterkühlung verwandt wurde als nach 30 Minuten bei normaler Körpertemperatur. Im weiteren Zeitablauf kam es zu einer progressiven Abnahme dieser Schutzwirkung, jedoch ließ sich eine gewisse Schutzwirkung auch noch nach einer Spanne von 4½ Stunden Stillstand nachweisen. Es wurde weiter berichtet über die Korrelation zwischen diesem biochemischen Befunden und dem Beobachtungen der Myocard-Tätigkeit. Es wird angenommen, daß die geringere Schädigung der Myocard-Funktion nach hypoxämischem Stillstand herrühren könnte von der Aufrechterhaltung einer normalen Körpertemperatur mit selektiver Hypothermie des Myocards.

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STUDIES OF FALLOT-TYPE COMPLEX

Clinical, angiocardiographic, electrocardiographic, vectorcardiographic and hemodynamic data concerning patients with tetralogy of Fallot showed that the tetralogy of Fallot must be regarded as a part of a large "spectrum" syndrome (the complex of the Fallot type) which includes the following six groups: 1) classic tetralogy of Fallot; 2) extreme tetralogy of Fallot; 3) acyanotic tetralogy of Fallot; 4) stenosis of the outflow tract of the right ventricle or pulmonary stenosis with interventricular septal defect and no overriding of the aorta; 5) partial transposition of the great vessels with stenosis of the outflow tract of the right ventricle or pulmonary stenosis and interventricular septal defect; 6) single ventricle with pulmonary stenosis. There is a common anatomic denominator: the existence of interventricular septal defect and stenosis of the right ventricular outflow tract or pulmonary stenosis. The groups differ from one another only in the anatomico-functional interrelations of these two factors. The third factor (aortic overriding) may be absent. All groups show a comparable clinical and pathophysiologic picture.

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INTRALOBAR PULMONARY SEQUESTRATION

The site of origin of the anomalous artery in pulmonary sequestration is usually the descending aorta immediately above the diaphragm. Origin below the diaphragm, usually from the abdominal aorta, is less common, occurring, however, in almost one fourth of the cases. Vessels arising from the intercostal arteries are more rare. Multiple tributary vessels, sometimes as many as five or six, have been recorded in at least 17 instances.

The course of anomalous vessels is quite variable, but most commonly they enter the lung through the pulmonary ligament. They may, however, be encountered on the diaphragmatic and lower posterior surfaces of the lower lobes in addition to the mediastinal surface. In almost all cases, the pleural space is obliterated by adhesions in the region of the sequestration, making identification of the tributary vessel difficult. In some cases, there are projections of pulmonary tissue along the anomalous artery into the mediastinum, tending to obscure the vessel and making its dissection hazardous. The caliber of the aberrant artery may be surprisingly large, especially in the young children reported.

Veins accompanying the anomalous artery and which join in the systemic return to the right heart have been described in only six instances, including the presently reported case. These veins have generally been considerably smaller than the artery, suggesting that only a portion of the venous blood returns from the sequestration to the right heart and that some at least enters the pulmonary venous return to the left side of the heart. In the more usual situation, i.e., without systemic venous branches, almost all the venous return is by way of pulmonary veins, thus producing a systemic arterial-left atrial shunt. If the details of the anomalous vessel or vessels are known, a safer surgical attack may be planned. If the anomalous artery originates from the artery itself, dissection and mobilization of the aorta sufficient for the possible emergency application of a suitable clamp proximal to the origin of this vessel are indicated. If the vessel originates from an intercostal or other artery appropriate proximal control should be gained *prior* to the dissection of the anomalous artery and the lobe itself.

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Isolated Total Anomalous Pulmonary Venous Drainage

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Anomalous pulmonary venous drainage is the condition in which blood leaving the lungs returns via systemic veins, or directly, to the right atrium. Complete anomalous connection of the pulmonary veins occurs as the only important abnormality of the cardiovascular system in some cases, but in others, additional congenital defects of the heart and great vessels are also present.

Classification

Anomalous pulmonary venous connections may provide channels for partial or for complete return of blood from the lungs to the right atrium. These are sometimes the only anomalies, but they also may be part of a complex of abnormalities. The isolated partial anomaly occurs in approximately 0.5 per cent of persons, but among patients with additional cardiovascular anomalies, partial abnormal pulmonary venous drainage is more common. About 15 per cent of patients with defects of the atrial septum requiring surgical therapy also have partial anomalous pulmonary venous connections.

There are approximately 100 previously reported cases of isolated total anomalous drainage,** but only one-half as many cases of the total anomaly associated with congenital cardiac abnormalities are recorded.[1]

This general orientation leads to the convenient grouping of the cases of total anomalous venous drainage presented by Darling, *et al.*,[2] based upon the level of the junction of the anomalous drainage channels with the systemic circulation.

Group	Level	Site of Connection	Distribution† in 103 Cases
I	Supracardiac	A. Left Superior Vena Cava or Left Innominate Vein	46
		B. Right Superior Vena Cava	11
II	Cardiac	A. Coronary Sinus	16
		B. Right Atrium	15
III	Infracardiac	A. Portal Vein	9
		B. Ductus Venosus	2
		C. Inferior Vena Cava	1
IV	Mixed	A. Superior Vena Cava and Right Atrium	1
		B. Coronary Sinus and Left Innominate Vein	1
		C. Inferior Vena Cava and Left Innominate Vein	1
			103

†Adapted from Keith.[1]

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**A patent foramen ovale is essential in all cases of total anomalous drainage, and it is implied in spite of the adjective "isolated." The latter term indicates absence of additional significant defects of the cardiovascular system.

Embryology

In the normal development of the pulmonary veins, the splanchnic plexus which surrounds the foregut communicates with the anterior cardinal, posterior cardinal, and umbilico-vitelline veins. Subsequently, a vascular channel forms to connect this plexus with the developing cardiac atrium and this is followed by disappearance of the connections between the splanchnic plexus and the cardinal and umbilico-vitelline veins. Meanwhile, growth of the lung buds extends into the splanchnic plexus and this plexus is established as the drainage system for the lungs. The single venous trunk between the lung buds and the left atrium is incorporated into the wall of the atrium as this latter structure enlarges, and as the single trunk is completely absorbed into the atrial wall, the four individual pulmonary veins come to have their own openings into the left atrium, thus establishing the normal postnatal condition.

The embryological basis for total anomalous pulmonary venous return results from retention of a connection with one of the anterior cardinal veins (which become the innominate veins and coronary sinus), with the umbilico-vitelline veins (which become the hepatic and portal veins), or because the venous trunk which connects with the developing atrium is incorporated into the right atrial wall rather than the left atrial wall.[3]

Pathology

In nearly all cases of the anomaly, the four pulmonary veins unite into a common trunk which proceeds to its union with the systemic vein or right atrium. Rarely, two or more veins progress to the right atrial wall or to veins at the supracardiac level. There are only three recorded instances of the connections being at two different levels.

Because all venous blood, both systemic and pulmonary, returns to the right atrium this chamber is invariably larger than the left. Usually the volume of the right chamber is 2 to 5 times that of the left. The left ventricle is also somewhat smaller than the right, but the thickness of the myocardium of each is similar. The mitral valve orifice, like the chambers of the left side of the heart, is smaller than usual.

The aorta and pulmonary artery are approximately the same size in about half the cases. In the others, the pulmonary artery is at least one-third again as large as the aorta.[4]

Diagnosis

The usual history of infants with this condition is as follows: health has been fairly good with essentially normal activity until a terminal episode begins with the development of cyanosis and dyspnea. When cardiac failure becomes manifest, it progresses rapidly to death.

In spite of the essential patent foramen ovale and the systemic circulation of some blood which has not cycled through the lungs, cyanosis is only slight or absent in nearly all patients until the terminal phase. Cyanosis is frequently first observed during episodes of crying or exertion. The oxygen saturation of arterial blood in thirteen patients was

recorded by Keith, *et al.*;[4] it was 63 per cent in one patient who was cyanotic, while in the others it ranged from 80 up to 95 per cent. The majority were in the range where cyanosis would not be recognized.

Heart murmurs were present in two-thirds of the infants under three months of age who were observed by Keith, and among the ten patients who had audible murmurs the sound was most commonly a short systolic one of moderate intensity between the second and fourth intercostal spaces adjacent to the sternum. Murmurs of this type were present in nine of the ten, and four of the nine also had a diastolic murmur in the fourth left intercostal space between the cardiac apex and the sternum. The tenth patient, a boy 3½ years old, had a soft continuous murmur over the region of the pulmonic valve and partway down the left border of the sternum. Three additional children were observed subsequently with similar murmurs. All four of these patients had abnormal pulmonary venous drainage into the left innominate vein.

Radiologic examination is extremely useful in the cases in which the pulmonary veins connect with the left innominate vein. After the first few months of life, there is widening of the mediastinal shadow above the heart so that the heart and this shadow together appear like the figure eight. One author has referred to this as a "mediastinal mustache," another as a "snowman" appearance. The enlarged heart shadow in cases where the pulmonary veins enter the coronary sinus, right superior vena cava, right atrium, inferior vena cava, portal or hepatic veins is not diagnostic. In occasional instances of venous connection with the coronary sinus, a "box-like shelf" occurs at the upper right border of the heart shadow. When present, this is said to be characteristic of such abnormal drainage.[5]

FIGURE 1 (Case 1): Postero-anterior film of chest taken one and one-fourth years prior to death. The "Figure 8" shadow of the heart and suprajacent vessels is characteristic. Increased vascularity of pulmonary hilar region.

Less often, the connection is via a trunk to an infracardiac vessel (Group III). These hearts are usually of normal size. Patients with infracardiac drainage have increased density of the lung fields, presumably reflecting pulmonary hyperemia, and this has aided some radiologists to consider the diagnosis from the chest films.

Angiocardiography may yield diagnostic information in cases of Group I, does not define the anomaly in Group II, and has not been reported in any case of the Group III type.

At fluoroscopy, the observation is often made that in spite of the prominent hilar vascular shadows, there is relatively little pulsation so that the enlargement may be recognized as being due primarily to venous rather than arterial engorgement.

Cardiac catheterization usually reveals elevation of the right atrial and ventricular pressures, although there are occasional patients with normal pressures. The pressure in the pulmonary artery is only slightly lower than that observed in the right ventricle. The oxygen saturation of blood in the right atrium is greater than normal, and passage of the catheter into the appropriate orifice may reveal the source of the oxygenated blood and hence the abnormal pulmonary venous connection. However, proof that the anomaly is a total one is not established by this procedure, since anomalous connection of a single vein can yield the same results.

The dilution curve of Evans blue dye in arterial blood following injection into a systemic vein is marked by a prompt appearance of dye shunted through the foramen ovale and a second rise in concentration as that portion circulated through the lungs is recirculated into the systemic vessels.[4] However, this shunt pattern may be obscured in cardiac failure.

Presentation of Cases

The following case, an example of total anomalous connection via the left innominate vein, is noteworthy because the patient survived until she was 43 years of age. At the time of death, she was older by 16 years than any previously described patient with this condition.

Case 1: The final admission to the hospital of this 43 year-old patient was on January 20, 1959, for somnolence and jaundice.

Medical records of this patient date back to the age of seven, at which time her pediatrician had referred her to an internist for evaluation of slight cyanosis, cardiac enlargement, and a heart murmur. The patient had observed no related symptoms and the cardiac murmur is not described. Right axis deviation was indicated by a three lead electrocardiogram, while fluoroscopic examination revealed enlargement of the heart and hilar vessels. The internist saw her again when she was eleven years old and observed slight cyanosis, but there was no congestive failure nor digital clubbing. The heart was enlarged with bulging of the precordium. A faint systolic thrill and a grade III systolic murmur were noted in the upper left parasternal region over the second and third intercostal spaces.

At age 31, the patient was admitted to the hospital for evaluation of cardiac status. Since she had become addicted to alcohol, icterus which was present was ascribed to dietary deficiency and alcoholism. A grade III systolic murmur was present over the base of the heart bilaterally and it was also heard over the back. An electrocardiogram revealed evidences of right ventricular hypertrophy and incomplete right bundle branch block. Chest films indicated a large heart with the "figure eight heart shape as in abnormal venous return" (Fig. 1). Additionally, fluoroscopy indicated that the predominant pulmonary hilar vessels did not pulsate excessively.

Her nutritional habits continued to be poor and she was admitted to the hospital on several occasions prior to the last admission for treatment of hepatic cirrhosis. Approximately one month before her last admission, she again had begun to consume large amounts of alcohol and in the few days before admission, there had been marked bruising of the skin and bleeding from the gums. Jaundice in varying degrees had been present for a year prior to this last admission. The cardiac murmur was noted and a forceful apical thrust was described. The heart rate at this time was 134 per minute and the blood pressure was 130/80. The lower edge of the liver was 10 cm. below the costal margin.

Her temperature rose rapidly to 104.6 degrees F., she became completely unresponsive, and death occurred eight hours after admission.

NECROPSY (E.H. 59-A-10)

The body was poorly nourished and the skin was greenish yellow. The globoid heart was estimated to weigh 400 gm. The right atrium and ventricle were unusually prominent, and were dilated to approximately three times the volume of the corresponding left chambers. The myocardium of the right and left ventricles was 7 mm. and 9 mm. in thickness respectively. The left atrial and ventricular chambers were slightly smaller than usual. The patent foramen ovale, septum secundum type, was 2.8 x 2.4 cm. (Fig. 2).

The right innominate vein was normal. The left innominate vein was approximately twice the diameter of the right, and in addition to receiving the usual veins of the left side of the neck and left upper extremity received a large common pulmonary venous trunk. The latter arose in the region of the hilum of the right lung by coalescence of the veins of the upper and lower lobes, crossed the midline dorsal to the parietal pericardium and anterior to the esophagus and aorta, and was joined by a large vein formed by the veins from the upper and lower lobes of the left lung. Thus, the veins from both lungs connected with the right atrium via the left innominate vein and superior vena cava. The coronary arteries and aorta were unchanged and the latter was 4.5 cm. in circumference. The circumference of the pulmonary artery was 5.5 cm. and a few atheromatous plaques were present in its intima.

The lungs showed no abnormalities other than the vascular ones previously described. The liver weighed 1755 gm. and had coarsely nodular surfaces.

There was an erosion of the mucosa of the cardia in a region 8 x 4 mm. and hemorrhage was present in the mucous membrane adjacent to this erosion. The stomach and intestines contained approximately 1000 ml. of partially clotted thick dark red blood.

Microscopically, the branches of the pulmonary artery were approximately half again the expected diameter and their walls were somewhat thicker than usual.

ANATOMICAL DIAGNOSIS

Congenital anomalies of cardiovascular system, with anomalous connection of all pulmonary veins to left innominate vein; widely patent foramen ovale; hypertrophy and dilatation of right chambers of heart; nutritional cirrhosis of liver; ascites; icterus; erosion of mucosa of the cardia, with massive hemorrhage.

In total anomalous venous drainage, the likelihood is greater that the common pulmonary venous channel will join a derivative of the anterior

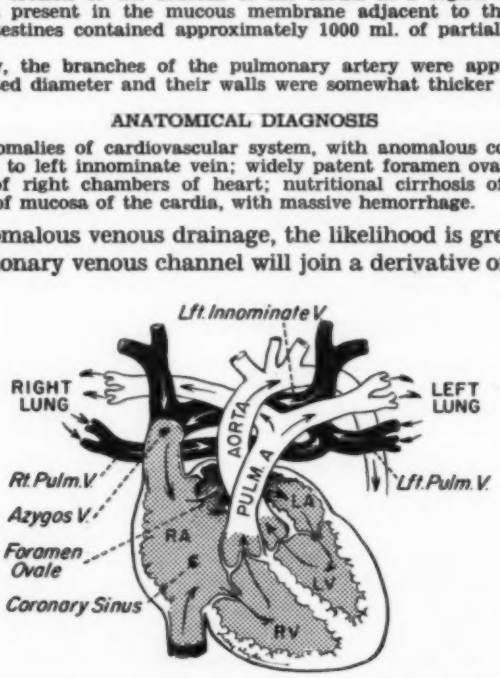

FIGURE 2 (Case 1): Diagram of heart and great vessels to illustrate route of pulmonary venous return. Not illustrated is the relatively large size of the pulmonary artery as compared to the aorta.

cardinal than a derivative of the posterior cardinal veins. Our second case is of the latter type.

Case 2: This patient was a seven day-old white male infant when he was admitted to the hospital because of "somnolence, irregular respirations, and poor feeding." The pregnancy and labor had been uneventful and the infant, which weighed five pounds thirteen ounces at birth, was described as lethargic following delivery and at twenty-four hours, was slightly icteric. The Coombs test was negative. Serum bilirubin concentration rose to 12 mg./100 ml., but then began to recede and the infant had been discharged at the age of five days in apparently good condition. At home, the infant drank only small amounts of milk. He was always somnolent, and this led to re-hospitalization for additional study. The only abnormality noted on admission was mild jaundice. Routine laboratory work yielded normal results. The cardiac shadow was not enlarged, and chest films were interpreted as diffuse pulmonary edema, more marked in hilar than peripheral regions, due to "some unrecognized congenital heart disease." His condition was poor, and the possibility of brain damage was considered. At the age of 18 days, he was transferred to a hospital for children, where the heart sounds were clearly audible, without murmurs and the heart was not enlarged. The lungs were clear by auscultation. The lower edge of the liver was 1 cm. and the lower edge of the spleen 2 cm. below the costal margin. By chest film, the cardiac shadow was normal in size and shape, while the lung fields were described as "homogeneously dense, suggesting diffuse atelectasis." While in the hospital, a machinery-like bruit was noted anteriorly and posteriorly over the chest, most prominent over the mid-epigastrium. The lower extremities developed pitting edema. There were episodes of shallow slow respiration in which the infant was described as appearing moribund, and during one of these he expired at the age of 28 days.

NECROPSY (C.H.E.B. 59-48)*

The well-developed body was poorly nourished and was 52 cm. long. There was pitting edema of the skin of the lower extremities. The lower edge of the liver was 6 cm. below the costal margin.

The estimated weight of the heart was 40 gm. The right atrium and ventricle were dilated. The foramen ovale was 9 x 7 mm. and the ductus arteriosus was 2 mm. in diameter. Pulmonary veins from each lobe joined together to form a common trunk posterior to the heart and the trunk penetrated the diaphragm posterior to the vena cava. This vessel was 6 mm. in diameter. It joined the vena cava in the region where the hepatic vein entered that vessel.

The myocardium of the right ventricle was 6 mm. and of the left 5 mm. in thickness. The left atrium and left ventricle had approximately half the volume of the chambers of the right side of the heart, but they were reasonably near the expected size for the age and size of the patient.

The lungs were reddish purple, relatively firm, and diffusely boggy.

The liver weighed 108 gm. and like the other organs of the abdomen was hyperemic.

ANATOMICAL DIAGNOSIS

Congenital cardiovascular disease with total anomalous pulmonary venous connection with inferior vena cava, atrial septal defect; patent ductus arteriosus; cardiac hypertrophy and dilatation; passive hyperemia of viscera.

The third case is one in which the pulmonary veins, derived from the splanchnic plexus, connected with the umbilical-portal veins, also a relatively rare route for abnormal pulmonary drainage.

Case 3: Following a normal pregnancy and delivery, this male infant had done well until three or four days prior to admission to the hospital at the age of 21 days, when exertional cyanosis was observed. Two days prior to admission, the baby was examined by a physician and an electrocardiogram and chest films were made. The only abnormality of the cardiogram was non-specific flattening of the T-waves of standard leads I and II, while the chest film indicated slight enlargement of the right side of the heart and increased pulmonary vascular markings. When the infant entered the hospital, he was described as well developed and well nourished, the pulse rate was 120 and the respiratory rate 24 per minute. The skin was bluish gray. A grade II diastolic murmur was heard over the base of the heart, and soft posterior basilar rales were present bilaterally. The liver edge was 3 cm. below the right costal margin.

The infant was given stimulants and an endotracheal tube was passed so that positive pressure breathing could be instituted. These measures were to no avail and the baby died 35 minutes after admission to the hospital.

*Necropsy by Dr. A. J. McAdams.

NECROPSY (C.H.E.B. 58-73)**

The well-developed and well-nourished body was 53 cm. long, and the only external abnormality was slight edema of the scrotum. The viscera were in their usual places and the body cavities contained no excess of free fluid.

The heart was estimated to weigh 28 gm. The right atrium and right ventricle were dilated, while the cavities of the left atrium and ventricle were slightly smaller than usual, so that the volumes of the former were estimated to be four times those of the latter. The patent foramen ovale was 1.5 x 1.0 cm. The ductus arteriosus admitted a small probe, but was almost completely closed.

The pulmonary veins arose as usual from the two lungs, and the four veins united into a common trunk behind the pericardium (Fig. 3). This trunk, which was 4 mm. in diameter, progressed caudally through the membranous portion of the diaphragm to enter the liver where it drained into a venous sinus approximtaely 1 cm. in diameter. The sinus, in turn, connected with the portal vein. The vascular sinus also received the umbilical vein, the luminal diameter of which was reduced to less than 1 mm. From the vascular sinus, six vessels ranging from less than 1 up to 2 mm. in diameter penetrated the substance of the liver. The communication to the portal vein had an internal diameter of approximately 4 mm.

The lungs were average in size and the only gross abnormality noted was accentuation of the lobular pattern.

The only lesion observed among the abdominal organs was a circumscribed reddish brown nodule 1 cm. in diameter within the substance of the pancreas. The contents of the cranium were normal.

The microscopic examination revealed only two remarkable facts. A thin layer of myocardial fibers surrounded the left superior pulmonary vein with some thickening of the subendothelial connective tissues of this vein, and the slide of the pancreas revealed that the nodular lesion was an adenoma which contained beta granules.

ANATOMICAL DIAGNOSIS

Congenital cardiovascular disease, with total anomalous pulmonary venous connection to umbilical and portal veins, and atrial septal defect; patent (partially closed) ductus arteriosus; passive hyperemia of viscera; small benign islet cell adenoma of pancreas.

Discussion

Nearly all persons with this anomaly die in infancy and the nature of the anomaly is determined only rarely prior to autopsy. Among the 58 cases tabulated by Keith, *et al.*,[4] 80 per cent of the patients died during their first year and only one survived the first decade. This exception was a patient 27 year old at the time of death. Among the 17 previously unreported cases described by Darling, *et al.*,[2] only three had survived more than a year, two of them dying at the age of 20 months and the third at

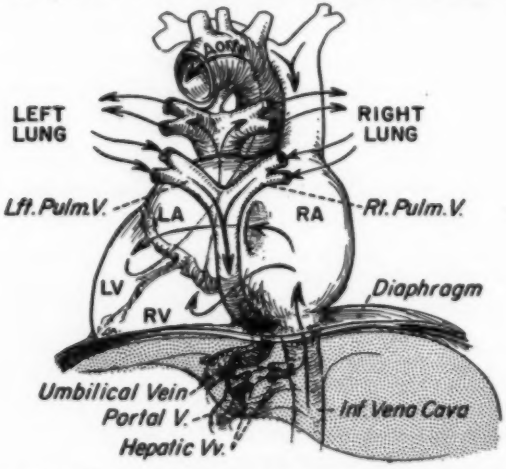

FIGURE 3 (Case 3): Diagram illustrating route of pulmonary venous drainage. The capillaries of the portal circulation are represented by two small arrows directed toward the hepatic vein.

**Necropsy by Dr. W. M. Palmer.

the age of four years. Two of our patients survived only a few weeks, while the third died of unrelated causes (alcoholic hepatic cirrhosis with gastric hemorrhage) at the age of 43 years.

It is possible that increased cognizance of the condition will lead to diagnosis and surgical correction in a significant proportion of these patients in future years.

The principles of treatment have been summarized by Keith[1] and they include the requirements that the common pulmonary vein be anastamosed to the left atrium, the connection between the common pulmonary vein and the systemic venous system be obliterated, and the defect of the interatrial septum be closed.

A number of attempts have been made to correct this anomaly and a few have yielded successful results. The most comprehensive discussion of surgical therapy at present is by Bahnson, Spencer, and Neill.[5]

SUMMARY

The development of anomalous pulmonary venous connections with the right atrium is briefly reviewed and the several types of this anomaly are described. Methods useful in diagnosis include chest films, angiocardiography, fluoroscopy, cardiac catheterization, and the dilution curve of dye in peripheral arteries or capillaries following an intravenous injection.

Three new cases are added to the 103 previously reported instances of isolated total anomalous pulmonary venous return.

ACKNOWLEDGMENT: The records pertaining to Case 1 were kindly supplied by Dr. Charles Peacock. Opportunity to examine the specimens and review the records from Cases 2 and 3 was through the courtesy of Dr. A. J. McAdams.

RESUMEN

El desarrollo de conexiones venosas pulmonares anómalas con la aurícula derecha se revisa brevemente y se describen las anomalías en sus varios tipos.

Los métodos útiles para el diagnóstico incluyen: radiografía de tórax, angiocardiograma, fluoroscopía, cateterización cardiaca, y la curva de dilución de colorante en las arterias periféricas o en los capilares después de una inyección intravenosa.

Tres nuevos casos se agregan a los 103 antes relatados de regreso venoso, pulmonar aislado total.

RESUMÉ

L'auteur fait une revue générale rapide des cas jusqu'alors décrits, oùse constitue un développement de connections pulmonaires veineuses anormales avec l'oreillette droite et il envisage les différents types de cette anomalie. Les méthodes nécessaires au diagnostic comprennent les clichés thoraciques, l'angiocardiographie, la radioscopie, le cathétérisme cardiaque, et la courbe de dilutions colorées dans les artères périphériques ou les capillaires à la suite d'une injection intraveineuse.

Trois nouveaux cas sont ajoutés aux 103 antérieurement rapportés.

ZUSAMMENFASSUNG

Es wird eine kurze Übersicht gegeben über die Entwicklung anormaler Verbindungen von pulmonalen Venen mit dem rechten Vorhof, und es werden die verschiedenen Typen dieser Anormalität beschrieben. Für die Diagnostik nützliche Verfahren bestehen in Thoraxröntgenaufnahmen, Angiocardiographie, Durchleuchtung, Herzkatheterisierung und der Kontrastmittel-Verteilung-Kurve in den peripheren Arterien oder Kapillaren im Anschluß an die intravenöse Injektion.

Es werden drei neue Fälle mitgeteilt zusätzlich zu den 103 zuvor veröffentlichten Befunden von isolierten totalen, anormalen Rücklauf der pulmonalen Vene.

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SUMMARY OF CURRENT THERAPY

The Significance and Treatment of Premature Systoles

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Premature beats of the heart, although usually of little clinical significance, might be of considerable importance if underlying cardiac disease is present. Premature beats, or extrasystoles, are cardiac contractions of ectopic origin which occur earlier than expected in the normal rhythm. The atria or the ventricles may be the site of origin of the premature contraction, or less commonly, the atrio-ventricular node. Premature contractions form the commonest of the cardiac arrhythmias and premature contractions of the ventricles are the commonest of the three types outlined above.

Etiology

A premature systole can be induced experimentally by stimulating the cardiac muscle at any time except during its phase of absolute refractoriness. They occur in the human heart as the result of some abnormal process of impulse formation, usually from stimuli which reflexly affect the vagus or sympathetic nerves. They may occur in association with organic heart disease, but more frequently in its absence. However, the presence of heart disease has a distinct tendency to increase the occurrence and frequency of premature systoles. Atrial premature systoles tend to occur in association with disease or enlargement of the atria, e.g. mitral stenosis or cor pulmonale. In non-cardiac patients, they may be of reflex origin initiated from the abdominal viscera. They may be due to some form of intoxication, e.g. digitalis, chloroform or cyclopropane anesthesia, hyperthyroidism, infections, emotional stress and conflict, mental and physical fatigue, irregular sleep, digestive disturbances, epinephrine, ephedrine, barium chloride, tea, coffee, alcohol, and excessive use of tobacco. Reduction of extra- or intracellular potassium following diuretic therapy or diarrhea predisposes to the formation of extrasystoles, especially in patients receiving digitalis.

Experimental premature systoles have been produced by stimulation of the hypothalamus and have occurred in man following brain lesions, indicating that in a minority of cases they may be of central origin. Atrial and ventricular premature systoles occur with high frequency during cardiac catheterization and cardiac surgery as a result of direct stimulation and manipulation of the heart. These might be followed by serious and often fatal ventricular arrhythmias. They may be the earliest evidence of myocardial involvement in diphtheria and are usually an indication of severe myocardial damage. They are common in myocardial infarction but uncommon in acute myocarditis due to rheumatic fever, viruses, and bacteria. If they do occur in rheumatic fever and other toxic

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states, they indicate severe myocardial involvement. Hypoxia due to chronic pulmonary diseases may be followed by premature systoles due to myocardial ischemia which disappear or decrease in frequency after the treatment of the primary pulmonary condition.

Premature systoles occur at all ages, but rarely in infancy and childhood. They have been recorded *in utero* and immediately after birth. After the age of 50, the frequency increases markedly; and after 70, they occur intermittently in almost all individuals.

Significance and Prognosis

The impairment of the heart's efficiency by a single premature systole is in direct proportion to its prematurity in time and, thus, the decrease in filling time. This is somewhat compensated by the post-extrasystolic pause, so that in most cases the overall function is not reduced significantly. However, a significant impairment may develop when several premature systoles follow each other, or in a bigeminal rhythm when each premature systole is interpolated. Then the cardiac output falls, the blood pressure drops, and heart failure may develop. In patients with stenosis of the coronary arteries, anginal pain may be provoked by a run of premature systoles due to poor filling of the heart and thus a drop in the rate of coronary flow. Multifocal premature systoles usually signify myocardial disease with the prognosis being that of the underlying pathology.

In a diseased myocardium, an extremely premature systole may result in ventricular fibrillation because the very end of the absolute refractory period constitutes the critical phase when any stimulus, such as a premature systole, may induce ventricular fibrillation.

Premature systoles are usually of no clinical importance, but they must be considered to be of significance following myocardial infarction. However, a diagnosis of organic heart disease must be based on symptoms or signs other than those of the premature systoles. The presence of premature systoles in the normal heart has no significance to longevity, insurability, or employability, even though the associated anxiety produces symptoms out of proportion to their prognostic significance.

Ventricular premature systoles are more serious if they arise from different sites in both ventricles (multifocal). In this case, they may denote advanced myocardial disease and impending ventricular tachycardia or fibrillation. Premature systoles due to digitalis toxicity are of clinical importance because they are potentially reversible. Bigeminal rhythm caused by premature systoles are commonly due to digitalis intoxication. When they occur with small doses of digitalis, they usually signify an unfavorable course. Atrial premature systoles may herald the onset of more serious atrial arrhythmias such as flutter, tachycardia, or fibrillation.

Treatment

A. General: Premature systoles are usually asymptomatic, requiring no treatment. If they are discovered during a routine physical examination and the patient is unaware of them, nothing should be said to the patient to draw his attention to them. If the physician feels he should

tell the patient, the significance of their benignity must be stressed. The physician must convince the patient that he has no heart disease and his activities need not be restricted.

However, treatment is indicated when the symptoms due to premature systoles are distressing to the patient in spite of reassurance. The patient should obtain adequate sleep and relaxation. A simple bedtime sedative often prevents the most disturbing arrhythmias. A well-balanced diet is offered, with control of constipation. Disease of the biliary tract should be treated and corrected, as should any foci of infection. Emotional stresses should be eliminated if possible. To this end, mild daytime sedation with phenobarbital or tranquilizers may be useful.

Tobacco, coffee, and alcohol should be eliminated for a trial period to see if they are a causative factor. If bigemini occurs during digitalis therapy, it must be temporarily discontinued. The treatment of hypoxia due to chronic pulmonary disease by such methods as intermittent positive pressure breathing (IPPB), bronchodilators, and measures to remove or reduce excess mucous in the bronchial tree may be instrumental in reducing premature systoles due to the hypoxic stimuli.

B. Specific

1. Procaine amide (Pronestyl): Procaine amide is most effective in the treatment of ventricular premature systoles. It acts by depressing myocardial activity and, in this respect, is similar to quinidine. It raises the ventricular threshold to stimulation, prolongs ventricular conduction, and increases the refractory period. The action on atrial muscle is similar but less pronounced. Procaine amide is given orally in an initial dose of 0.75 to 1.25 gm. followed by 0.5 gm. every four to six hours. When the premature systoles are controlled, the dose is slowly reduced to 0.5 gm. three or four times daily. Subsequently, a maintenance dose of 0.25 gm. four times a day is usually effective. If the initial schedule is ineffective, 1.0 gm. may be administered every four hours until the premature systoles are controlled or until there are toxic symptoms; then a maintenance dose is prescribed.

2. Quinidine sulfate: Quinidine acts by depressing myocardial excitability. Following an initial test dose of 0.2 gm. (3 grs.), 0.3 to 0.6 gm. (4½ to 9 grs.) is given three to six times daily for one week. If the premature systoles disappear, the exact maintenance dose may be determined by gradual reduction of the dosage. Eventually, the drug should be discontinued if possible.

3. Digitalis: Sometimes digitalis in doses of 0.1 gm. three times a day for three days, followed by 0.1 gm. daily, is effective in controlling premature systoles whether heart failure is present or not. Occasionally, it is effective when quinidine has failed. By improving congestive failure, it makes the heart less susceptible to the development of premature systoles by improving systemic and coronary hemodynamics.

4. Potassium salts: Potassium chloride, phosphate, or acetate is often effective in controlling premature systoles, especially if digitalis intoxication is present. The dose is 2 to 4 gm. (30 to 60 grs.) three or four times daily. For intravenous administration, an ampoule of potassium chloride

with 3.7 gm. (50 m.Eq.) is dissolved in 500 or 1000 cc. 5 per cent dextrose in water and given over a minimum period of two hours. Potassium salts should not be given, or only with caution, to patients with renal damage.

5. Magnesium salts: Twenty cc. of 20 per cent solution of magnesium sulfate injected rapidly intravenously abolishes or reduces the frequency of bigemini due to digitalis intoxication.

6. Rhythmol: Rhythmol is a new drug which has been shown to be very valuable in the treatment of premature contractions. Its properties are similar to those of quinidine, but toxic effects are less. The oral dose of 200 mgm. four times a day may be gradually increased until the arrhythmia stops or side effects appear. For intravenous use, 100 mgm. can be repeated every ten minutes to a total of 500 mgm.

7. Vasopressors: Vasopressor drugs are effective in terminating premature contractions in the ischemic heart due to hypotension from various causes such as myocardial infarction. They should be used only for the treatment of severe hypotension. If the pressor response to the vasopressor drug is too rigorous, more serious ventricular arrhythmias may result and, therefore, constant supervision in the control of the rate of infusion of the drug is essential.

ACHALASIA OF THE ESOPHAGUS IN CHILDREN

Achalasia or cardiospasm is a rare condition in children and there is little concerning the condition in this age group available in the medical literature. Six cases are reviewed.

Strip biopsies were secured from the lower esophagus in two patients and these contained no ganglion cells. Similar strips of tissue were removed from the normal esophagus of patients at postmorten examination and these contained numerous ganglion cells. Peristaltic studies were made in the two patients operated upon and these demonstrated good propulsive function in the esophagus.

The similarity of this condition to that in adults is indicated. Pathologic studies in adults have been made by several investigators and a degenerative lesion of Auerbach's plexus of the lower esophagus has been demonstrated. It is postulated that in children the defect is the same except that the lesion is congenital in origin. The diagnosis of achalasia in children is based on the clinical history and roentgenographic studies. Occasionally, the diagnosis can be established on a chest film showing widening of the mediastinum. Two of our cases were correctly diagnosed on a simple chest roentgenogram. On the barium swallow, there is smooth narrowing at the cardia with dilatation which is greatest in the lower half. Depending upon the severity and duration of the disease, the entire esophagus becomes dilated and tortuous. Occasionally, esophagoscopy is of value in differentiating achalasia from stenosis due to peptic esophagitis or chemical burns, although, generally, achalasia creates less of an acute problem and does not have a comparable clinical history. The effectiveness of dilatation in four cases of surgery on the lower esophagus in two cases is given on the basis of two to eight-year follow-up studies.

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ELECTROCARDIOGRAM OF THE MONTH

Edited by Stephen R. Elek, M.D.

Wenckebach Block of Sino-Atrial Conduction*

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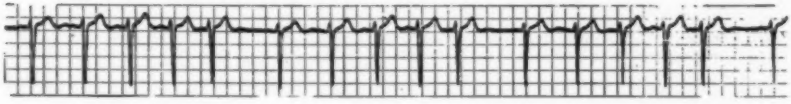
This electrocardiogram, a continuous strip of lead V_2 was obtained from a 62 year-old man who complained of syncope. This patient was a known hypertensive with a diaphragmatic infarct suffered two years prior to this admission. At the time he came into the hospital, his admission blood pressure was 220/110 mm.Hg. The chest x-ray film showed left ventricular hypertrophy. He had been on no previous cardiac medication. The tracing reveals three sequences of five beats separated by a pause. In each period, progressively shorted P-P intervals are seen, the last P-P interval preceding the pause is shorter than the first following it, and the pause measures less than the sum of any two preceding consecutive P-P intervals. This arrhythmia may then be interpreted as a Wenckebach block of sino-atrial conduction and is explained by the fact that as the sino-atrial conduction time becomes progressively longer, the increment of lengthening becomes progressively less. This causes an acceleration of the atrial rate preceding the dropped beat.

In sino-atrial block, the conduction of the normal impulse from the sinus node is impaired so that the atria are not normally activated. As in atrio-ventricular conduction, the block may be complete with sinus arrest or may be incomplete with the appearance of Wenckebach periods.

Sino-atrial block with Wenckebach periods must be differentiated from sinus arrhythmia and from non-conducted auricular premature systoles. In sinus arrhythmia, the changes in P-P intervals are phasic and much more gradual than in Wenckebach sino-atrial block. Non-conducted auricular premature systoles may be distinguished by the appearance of the premature P wave in the T wave or S-T segment of the beat preceding the pause.

Sino-atrial block may be caused by digitalis, quinidine, organic disease of the sinus node or by any factor capable of producing vagotonia. Advanced sino-atrial block may be associated with syncope and even Stokes-Adams seizures.



V_2

*From the Dr. Charles Block Cardiac Laboratory, Newark Beth Israel Hospital.

Editorial

A New Concept of Emphysema

In the last few years, so much has been written on emphysema that another article on the subject must indeed be unusual to warrant editorial comment. I believe that the recent contribution, "The Problem of Pulmonary Emphysema; the Missing Link between Structure and Function," by Rappaport and Mayer[1] appearing in *The Lancet* does fall into the category of the unusual.

In this article, they advance the view that the bronchiolo-alveolo-capillary structures could actively participate in the creation, maintenance and adaptation of the diffusion surface to the constantly changing requirements of gas exchange in the body. The nature of the activities of the bronchiolo-alveolo-capillary structures is accordingly the missing link between them and their special function, designated by the authors as "visceral lung function." This concept of the function of the lungs proper was presented previously by Rappaport in the January, 1954 issue of this journal.[2] Editorial comment in the same issue was then made by Mayer who has since collaborated in the application of this concept to the problem of emphysema.

Their exposition is not presented as a solution to the old problem of emphysema. Indeed, they are posing a new and perhaps even more difficult problem, namely: that of the missing link of the nature of visceral lung function. They emphasize that "visceral lung function" is no longer a mere theory since some of its basic assumptions have lately become demonstrated facts. Most recent physiologic studies revealed striking evidence of regional autonomy of so-called "alveolar ventilation and perfusion relationships," which proves this to be just the type of function postulated for lung function proper. Although, as the authors point out, only a mere beginning has been made in this field and much of the missing link is still to be found, yet from available data it is already possible to construct a reasonable concept of this primary function of the lungs and upon this basis, it is possible to make a fresh approach to the problem of emphysema.

The emphysematous state is described as developing through a two-fold process which lies in the nature of the structures and their function. In affected alveoli, the injury to the bronchiolo-alveolo-capillary structures (by biologic or physicochemical agents) results in cessation of diffusion surface creation, loss of septal partitioning, enlargement by coalescence and mechanical overexpansion due to increased effect of thoracic traction, as well as to relative narrowing of the air passages. In *affected alveoli,* this results in *progressive anatomic emphysema due chiefly* to mechanical overdistention. *Compensatory function involves functional overinflation of unaffected alveoli, depending upon the extent of lost function in affected alveoli.* With advance of the emphysematous state and diminishing reserves, both mechanical overdistention and functional hyperinflation continue to increase, each aggravating the

other. Finally, when reserves have become inadequate, anatomic emphysema can no longer be compensated for, pulmonary insufficiency prevails and the progress of pulmonary failure is imminent.

The emphysematous state then represents pulmonary insufficiency in the strict sense of this term which implies inadequate diffusion surface for gas exchange, either because of an insufficient number of air sacs available for normal function, or because of inefficiency of function in available functioning structures. In the origin of pulmonary insufficiency (by injury to a large proportion of structures or by inadequate compensation due to lack of reserves) these two causes are so closely linked that it is hardly ever possible to separate them.

In this new light, emphysema appears as a sequel to a great variety of pulmonary affections which are capable of injuring substantial numbers of lung structures and of reducing the normally large reserve. Accordingly, emphysema should be considered neither a primary disease nor a separate clinical or pathologic entity. There is only the emphysematous state which, despite variable origins, results in the same clinical picture of progressive chronic pulmonary insufficiency. This original concept affords explanations of many previously unexplained aspects of the etiology, pathology, pathogenesis, clinical and functional phases of emphysema.

This article presents a challenging and completely novel approach to the long standing problem of emphysema by way of a new line of study of pulmonary function. I feel confident that this new avenue of approach to pulmonary research will be trod promptly by our new generation of researchers, that the missing link will be found and may well prove to be the key to the solution of the problem of emphysema. These comments accordingly are intended to stimulate interest in such a study.

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SUGGESTION FOR IMPROVING IMMEDIATE AND LATE SURGICAL RESULTS FOR CARCINOMA OF THE BREAST

The author points out the importance of carcinomatous involvement of the pleura in numerous instances of mammary carcinoma which may follow radical resection of the primary neoplasm of the breast, regional glandular extirpation and post-operative x-ray therapy. In addition to the use of radioactive gold for the treatment of pleural carcinosis, the author advocates the prophylactic administration of Au^{198} intrapleurally following radical mastectomy.

Sattler, A.: "Ein Vorschlag zur Verbesserung naher und ferner Operations-resultate beim Mammakarzinom im Hinblick auf die Entstehung pleuraler Metastasen bildung," *Krebsarzt*, 16:4, 1961.

NEW COLLEGE OFFICERS ELECTED

The Executive Council, Board of Regents and Board of Governors held their annual meetings in New York City. Matters of policy, as well as reports of College councils and committees were discussed. The proceedings of these meetings and reports of the councils and committees will be published in subsequent issues of *Diseases of the Chest*. All of the councils and committees of the College held their meetings on Friday, June 23.

Reports of the President, Treasurer, Historian, Executive Director and chairmen of the Committee on Nominations and Committee on Bylaws were presented at the open administrative session on June 23. The following officers for the year 1961-1962 were elected:

Officers

President:	Hollis E. Johnson, Nashville, Tennessee
President Elect:	John F. Briggs, St. Paul, Minnesota
First Vice President	Charles K. Petter, Waukegan, Illinois
Second Vice President:	Alfred Goldman, St. Louis, Missouri
Treasurer:	Albert H. Andrews, Chicago, Illinois
Assistant Treasurer:	William E. Adams, Chicago, Illinois

Honorary Regents

	Edgar Mayer, New York, New York
	Dean B. Cole, Richmond, Virginia

Regents

District No. 2	Coleman B. Rabin, New York, New York
District No. 4	Edgar W. Davis, Washington, D. C.
District No. 6	Howard S. Van Ordstrand, Cleveland, Ohio
District No. 8	Charles A. Brasher, Mt. Vernon, Missouri
District No. 10	Johann L. Ehrenhaft, Iowa City, Iowa
District No. 14	Edward H. Morgan, Seattle, Washington
District No. 16	Hastings H. Walker, Honolulu, Hawaii
Historian	Carl C. Aven, Atlanta, Georgia

Governors

Alaska	James E. O'Malley, Anchorage
Delaware	Gerald A. Beatty, Wilmington
District of Columbia	Thomas W. Mattingly, Washington
Indiana	John V. Thompson, Indianapolis
Iowa	William B. Bean, Iowa City
Kentucky	John S. Harter, Louisville
Massachusetts	Dwight E. Harken, Boston
Missouri	David Nafe Kerr, St. Louis
Montana	Lloyd M. Taylor, Great Falls
Nebraska	Robert L. Grissom, Omaha
Nevada	Thomas F. Keyes, Las Vegas
New Hampshire	Francis J. Kasheta, Glencliff
New Mexico	Joseph E. J. Harris, Albuquerque
New York	Theodore H. Noehren, Buffalo
Ohio	Ray W. Kissane, Columbus
Oklahoma	Donald W. McCauley, Okmulgee
Oregon	William S. Conklin, Portland
Rhode Island	Frank A. Merlino, Providence
South Carolina	J. Gordon Seastrunk, Columbia
South Dakota	Stephen M. Brzica, Sioux Falls
Wisconsin	John Rankin, Madison

Governors in the U. S. Government Services

U. S. Navy	Joseph M. Hanner, Captain, USN, (MC) San Diego, California
U. S. Public Health Service	Robert J. Anderson, Washington, D. C.

Governors of the College in Canada

British Columbia	W. Elliott Harrison, Vancouver
Quebec	B. Guy Begin, Montreal

ALVAN L. BARACH, M.D. "Fabian Bachrach"

DR. ALVAN L. BARACH RECEIVES 1961 COLLEGE MEDAL

The College medal for meritorius achievement in diseases of the chest was presented to Dr. Alvan L. Barach at the 27th Annual Meeting of the College in New York City on June 25. The award was made by Dr. M. Jay Flipse at the Presidents' Banquet held in the Commodore Hotel.

Dr. Barach began his studies on respiratory physiology and their application to clinical medicine in 1920 at the Harvard Medical School and at the Massachusetts General Hospital. Since 1922 he has been engaged in research and practice in diseases of the chest at the Presbyterian Hospital and the College of Physicians and Surgeons, Columbia University, where at the present time he is Attending Physician in Medicine and Clinical Professor of Medicine Emeritus.

His investigations of the principles involved in the application of oxygen resulted in the development of the ventilated oxygen tent, oxygen masks, oxygen rooms, a variety of pressure breathing apparatus, chambers, hoods, and facial appliances. He introduced helium as a therapeutic gas for the treatment of asthma and obstructive dyspnea. In recent years his investigations have been concerned with the problem of retained secretions in the lungs. The development of mechanical coughing ("exsufflation"), techniques of increasing the efficiency of ventilation, patient controlled ventilation and the administration of "super-heated" aerosols have been employed in patients with bronchial asthma, pulmonary emphysema and other clinical entities. He has been especially interested in rehabilitation of the patient with pulmonary emphysema, especially the development by the patient of efficient methods of ventilation and exercise, and the use of portable oxygen apparatus during physical exertion.

In 1936 Dr. Barach received the Bronze Medal, Class I, for original investigation of helium and oxygen in various types of dyspnea by the American Medical Association; in 1938 the Scroll of Honor for meritorious research in clinical medicine and gas therapy by the International Anesthesia Research Society; in 1942 the Townsend Harris Medal, College of the City of New York; and in 1960 the Award of Merit of the American Association of Inhalation Therapists.

Dr. Barach was a responsible investigator in World War II in charge of the Aviation Research Laboratory and the high altitude chamber of Columbia University, conducting investigations on methods of increasing the resistance of the individual to low barometric pressures, including the application of pressure breathing.

He is the author of four books and several hundred papers on physiological and clinical aspects of chest diseases, including contributions to various textbooks. Dr. Barach is a Fellow of the American College of Chest Physicians and has served as chairman of the College Council on Research and as President of the Research and Education Foundation for Chest Disease.

SCIENTIFIC NEWS ITEMS FROM THE 27th ANNUAL MEETING*

American College of Chest Physicians

New Test for Chest Pain Problems

A thorough report on differential diagnosis of thoracic pain was given by a group of researchers headed by C. DuWayne Schmidt of the Mayo Clinic. They studied 514 patients with special reference to the role of abnormal esophageal motility in the provocation of chest pain. Clinical differentiation could not consistently be made between the pain of ischemic heart disease and of esophageal motility disorders. It was recommended that when patients present a diagnostic problem related to pain in the thorax, ischemic heart disease should be excluded even though the presence of esophageal disorders is proved. The ECG after exercise may be helpful in evaluation of such patients.

Respiratory Hazards of Space Fuels

Edward M. Cordasco, *et al.*, Niagara Falls, presented observations on patients exposed to inhalation of new high energy fuels used for stratospheric travel, such as boranes. Of 26 patients with acute diborane toxicity, 18 had respiratory tract involvement. Of 33 with subacute exposure to diborane, 8 became ill with symptoms referable to the lung. Seven per cent of 35 patients with decaborane had pulmonary symptoms. Exposure to pentaborane was followed by bronchopulmonary disease in 3 patients of 166 so exposed. All patients recovered completely from the effects of the aforementioned toxic inhalants.

A Variant of Tietze's Syndrome

Carabasi, Christian and Brindley, Temple, Texas, reported 89 patients with localized pain and tenderness in the anterior chest wall seen in a 15-month period. Site of pain and tenderness was over the third, fourth and fifth costosternal junctions. The condition is designated costosternal chondrodynia. They consider it a distinct clinical entity which differs from Tietze's syndrome by expansion of swelling by simultaneous involvement of several costosternal junctions and by its response to x-ray therapy.

Thoracic Sequels of Acute Pancreatitis

Fishbein, Murphy and Wilder of Baltimore have reviewed 155 cases of clinically proved pancreatitis. All of the patients had normal chest x-ray findings, either at the onset of illness or at a prior examination. They found that 22 patients (14.2 per cent) had x-ray findings of pleural effusion, pleural reaction, plate-like atelectasis, or basilar infiltrates. Nine of these reactions were in the left chest, nine in the right, and three bilateral.

Pulmonary Resection

A comprehensive review of the merits and demerits of apical and posterior segmental resection of the right upper lobe in 88 patients contrasted against a group of 97 patients treated by right upper lobectomy was given by Andrews, Marshall, and Christoforidis of Columbus, Ohio. There was a 63 per cent incidence of complications in those patients treated by segmental resection and 35 per cent in those treated by lobectomy. In 19 patients treated by segmental resection, the anterior segment collapsed and remained in this state, thus, in essence, producing a right upper lobectomy. It was suggested, in view of the higher morbidity and minimal effectiveness of the anterior segment, that right upper lobectomy is the procedure of choice in suitable cases of pulmonary tuberculosis.

The Menace of Esophageal Reflux

John Hines Kennedy, San Diego, reported on "silent" gastroesophageal reflux based on observations of 25 patients, all of whom sought medical attention because of symptoms referable to the lung, such as cough, expectoration, pulmonary hemorrhage and pain in the chest. Examination revealed evidence of bronchitis, bronchiectasis, unresolved pneumonitis or empyema secondary to gastroesophageal reflux with or without radiographically demonstrable hiatus hernia. The evidence of the latter was revealed only at the time the patients developed respiratory symptoms.

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*This is a new feature of this journal for the purpose of bringing most recent information promptly to the attention of our readers. Many of these items will be published in full in future issues of *Diseases of the Chest*.

J. ARTHUR MYERS, M.D.
Editor-in-Chief

Congenital Unilobar Emphysema

The report of Mercer, Hawk and Darakjian, Cleveland, was based on four cases of congenital unilobar emphysema treated at the Cleveland Clinic in recent years. The onset of the disease is usually in early infancy, but not at the time of birth. Symptoms are those of wheezing respirations and attacks of coughing, rapid breathing and cyanosis. Respiratory distress may be profound and death is the usual result in unrecognized cases. Treatment of the disease is surgical and most patients operated upon have recovered.

Surgery in Histoplasmosis

Beatty and his co-workers from Louisville, Kentucky, emphasized that resectional surgery in open cavitary histoplasmosis without antimycotic drug coverage is hazardous, with pneumonic spreads occurring frequently. Surgery appears relatively safe in the non-cavitary forms of pulmonary histoplasmosis. Also, surgical therapy of the cavitary forms with antimycotic drug therapy, amphotericin-B, before and after surgery, is safe.

Surgical Treatment of Pectus Excavatum

During the past seven years, 96 cases of pectus excavatum have been treated surgically by Colin S. Dafoe and Colin A. Ross of Edmonton, Canada. Correction of the deformity has been maintained utilizing a method devised by them. The results have been exceptionally good in 94 of their cases, even in adults with extreme degrees of deformity. In two infants, the result was not entirely satisfactory. One of these, at re-operation, obtained an excellent result. In addition, 50 cases of severe isolated stove-in chest injuries were treated satisfactorily by this method which permits early ambulation of the patient.

New Respiratory Stimulant

The effects of a new respiratory center stimulant, vanillic diethylamide (Emivan), have been studied by Sami I. Said and C. M. Banerjee, Richmond, Virginia, in 14 patients with obstructive emphysema, obesity or pulmonary fibrosis. In all but three patients, intravenous injection of a single dose of 25-50 mg. caused a significant lowering of arterial CO_2 tension and elevation of arterial O_2 tension. The hyperventilation appeared within 15-20 seconds and lasted for 5-10 minutes. Alveolar ventilation was increased almost two-fold as a result of a sharp increase in tidal volume. The three patients who failed to respond had advanced respiratory acidosis. Other effects of intravenous administration of the drug consisted of a moderate rise in arterial blood pressure, marked arousal, and, occasionally, transient dizziness and hot flushes.

ECG Patterns Simulating Infarction

Cesar Caceres, Washington, D. C., discussed constant association which exists between abnormal surface ECG patterns characteristic of those seen in conventional electrocardiograms of subjects with coronary artery disease and intracavitary evidence of premature depolarization. Local cavity "injury currents," when sustained, are also associated with evidence of premature depolarization of an area of myocardium. Observations suggest similar mechanisms of production may be attributable to abnormal electrocardiographic patterns in normal subjects, as well as to the patterns obtained in disease states. It would appear that without regard to etiology, varying degrees of premature depolarization of an area of myocardium or of an entire ventricle and the time lapse between atrial and ventricular depolarization are capable of producing many different types of abnormal electrocardiographic patterns.

Mechano-cardiac Pulsator: New Method

Philip Attalla, *et al.*, Chicago, devised a method by which adequate systemic circulation could be maintained by mechanical cardiac compression for as long as 120 minutes. For this purpose,a compressible rubber cuff, the mechano-cardiac pulsator, was designed. This consists of an inflatable compartment making possible selective pressure over the left ventricle and indirectly much lower pressure over the right ventricle, thus obtaining satisfactory high peripheral systemic and low pulmonic pressures. Long periods of massage were maintained without ill effect to the cerebral, coronary or pulmonary circulations. The myocardium could easily be restored to normal rhythm at the end of the procedure.

Antihypertensive Agent

Moyer and Brest, Philadelphia, report that guanethidine possesses a hypotensive potency similar to that of the ganglion blocking compounds. The antihypertensive effectiveness of the compound is significantly enhanced by the concomitant administration of thiazide derivatives. This new antihypertensive agent holds particular promise for those patients with the more severe degrees of diastolic blood pressure elevation. The lesser incidence of side reactions, lack of parasympatholytic effects, and prolonged therapeutic response constitute significant clinical advantages for guanethidine in comparison with the ganglion blocking drugs.

ECG Characteristics of Digitalis Intoxication

Alfred Soffer, Rochester, New York, analyzed the electrocardiograms of 11 patients who experienced digitalis intoxication. Such toxicity was characterized electrocardiographically by atrioventricular dissociation with non-paroxysmal nodal tachycardia and an AV nodal rate above 70. It was demonstrated in this series that awareness that digitalis in excess enhances impulse formation in AV junctional tissue can be of life-saving importance.

Idiopathic Myocardial Disease

Fowler, Gueron and Rowlands, Cincinnati, described 23 patients who had congestive heart failure without clinical or pathologic evidence of primary cause. Twenty of the patients were necropsied; three had a myocardial biopsy. The ages of these patients were from 18 months to 68 years at death; eight of the patients had heart failure for five years or more. All patients had left ventricular enlargement at necropsy. There was no evidence of coronary disease, myocarditis, or subendocardial fibroelastosis. Idiopathic myocardial disease is of clinical importance because it may simulate coronary artery disease, hypertensive heart disease, pericardial effusion, or rheumatic heart disease. The cause is unknown.

Isolated Ventricular Septal Defect

Lasser and Lasser, New York City, reported that of 43 patients in their series, those with isolated left ventricular hypertrophy (LVH), diastolic overloading (D.O.), as well as the ones with normal electrocardiograms, had normal or slightly elevated pulmonary artery pressures and small to moderate left-to-right shunts. Patients with LVH, D.O. plus RVH (right ventricular hypertrophy) had moderately elevated pulmonary artery pressures and moderate to large left-to-right shunts. Whenever right ventricular pressure exceeded 60 mm. Hg., LVH, D.O. pattern no longer appeared. Patients with advanced RVH and combined hypertrophy without evidence of LVH, D.O. had moderate to marked pulmonary hypertension. The pattern of LVH, D.O. is a distinct entity in isolated ventricular septal defect. Certain generalizations can be made regarding the relationship of the ECG with hemodynamic findings in ventricular septal defect; however, no completely predictable correlation could be demonstrated.

Thromboendarterectomy for Coronary Heart Disease

Charles P. Bailey and William M. Lemmon, New York City, presented a summary of their experience with their original, improved techniques of coronary endarterectomy. With adequate delineation of the coronary tree by cinecoronaryarteriography, exact diagnosis and localization of the lesion no longer present the previously nearly insuperable difficulties. New developments in microvascular surgery have made it clinically feasible to remove these potentially lethal lesions. By employing deep regional or total body hypothermia and complete cardiopulmonary bypass in properly selected cases, the intracoronary lesion can be removed successfully with re-establishment of essentially normal blood flow to the involved area of myocardium.

Renovascular Hypertension

According to Morton H. Maxwell, Los Angeles, current studies indicate that between 5 and 15 per cent of the hypertensive population has unilateral or bilateral renal arterial occlusive disease which is potentially surgically reversible. A combination of a radioisotope renogram and an intravenous pyelogram performed with rapid injection of the dye and with films at one-minute intervals for the first five minutes is without danger to the patient and will serve to distinguish differential variations in renal function in most instances. In some cases, however, the renal arteriogram is the sole means of detecting renal artery disease. Of predictive value in selection of patients for surgery on physiologic and clinical grounds are the tetraethyl ammonium chloride test and individual kidney function studies. A newer technique of performing individual kidney function tests utilizing comparative para-amino hippurate concentrations rather than sodium concentrations and urine volume has made this technique more sensitive and less fraught with technical error.

Surgery for Aortic Regurgitation

Fourteen patients with aortic regurgitation whose cardiac condition has been corrected surgically, employing an artificial plastic valve made from Teflon fabric and fashioned after the normal aortic valve, have been reported by Kay, Suzuki and Mendelsohn of Cleveland. There was no initial operative mortality, but a 20 per cent late mortality from complications of infection that the clinicians thought might be avoided in the future.

Thiazide Diuretics in Hypertension

Walter M. Kirkendall, Iowa City, stated that since the introduction of thiazide diuretics in 1957, they have been shown to be capable of reducing pressure in patients with most forms of hypertension. New analogues of the parent chlorothiazide molecule are more potent on a mg. per mg. basis and have a longer duration of action. Many have less carbonic anhydrase inhibiting effect. The mechanism of the depressor action of the thiazides is still uncertain. Initial reduction of blood volume is corrected after two to three weeks of continuous therapy. The thiazides have exerted their characteristic effects without development of tolerance during the several years which they have been used. There are relatively non-toxic agents. Hyperuricemia, hypokalemia and an occasional instance of hyperglycemia are side effects which have caused concern and/or aroused interest concerning the mechanism of action of these drugs.

Treatment of Rheumatic Myocarditis

Alvan R. Feinstein, Irvington-on-Hudson, New York, presented comments on the basis of personal observations in the therapy of rheumatic myocarditis. At least one-third of patients with identifiable rheumatic fever do not have carditis. They will respond well to any or no therapeutic regimen and will remain free of heart disease thereafter. Significant cardiomegaly, pericarditis and congestive heart failure occur almost exclusively in patients with significant murmurs. In patients *without* significant cardiomegaly, rheumatic heart disease remains in about 50 per cent of those with diastolic murmurs and in about 25 per cent of those with only organic apical systolic murmurs. In these patients, salicylates and steroids appear to have the same effects and there is no valid proof that either of these agents has better cardiac results than symptomatic therapy alone. In patients *with* significant cardiomegaly and/or congestive heart failure, steroids have not been demonstrably superior to salicylates in changing the *ultimate* cardiac prognosis, although steroids can sometimes be immediately life-saving in suppressing acute inflammation.

Treatment of Hypertension

Edward D. Freis, Washington, D. C., gave a critical review of this subject. He said that hydralazine (Apresoline) increased cardiac output, renal, hepatic and coronary blood flows, while total peripheral resistance decreased. Diastolic pressure is reduced. The acute side effects of headache, palpitation, and dyspnea on exertion can be minimized by gradual elevation of dosage. When given alone, oral reserpine reduces blood pressure only in a small minority of patients, but gains in effectiveness when used as an adjunct with other hypotensive drugs. A true reactive depression and occasionally suicidal depression may be precipitated. Other side effects include nasal stuffiness, increased appetite, bradycardia, nightmares and occasionally gastrointestinal bleeding. The drug, therefore, must be treated with respect and maintenance dosages kept as low as possible. Veratrum alkaloids produce a reflex decrease in heart rate and total peripheral resistance. Their clinical value in long-term therapy is limited because of the frequency of nausea, vomiting, hypotension and hiccough.

Swallowing Restored with Minimal Surgery

Henry J. Heimlich, New Rochelle, New York, succeeded in effectively relieving esophageal obstruction caused by inoperable carcinoma of the esophagus. He inserts a polyethylene tube through the carcinoma by means of an incision of the neck, or by means of a gastrotomy, depending on the level of the carcinoma within the esophagus. Thus, esophageal obstruction is overcome without subjecting the patient to the risks and discomforts of thoracotomy. The operation is of value, therefore, in the many cases where inoperability can be determined by the presence of cervical lymph node or distant metastases, invasion of the bronchus, or general debility. Radiotherapy and chemotherapy can be administered in order to deter the growth of the carcinoma, without fear that the esophagus will obstruct or after the course of therapy.

Ambulatory Treatment of Tuberculosis

S. Clive Cohen, Boston, reported on a study of 1,377 tuberculous patients under ambulatory care who are receiving or had been receiving specific chemotherapy. X-ray results showed that 16.0 per cent definitely improved, 72 per cent remained stable and inactive, 7.3 per cent worsened, 4.6 per cent were inconclusive because of lack of total information. Results of sputum and gastric cultures showed that 60.7 per cent were always negative, 24.7 per cent changed from positive to negative, 1.3 per cent changed from negative to final positive; they were unable to obtain conclusive information from 13.3 per cent of the patients because they could not raise sputum and did not come in for scheduled gastric examination. Resistant organisms were present in 1.3 per cent of the patients, no resistant organisms for 56.7 per cent and resistant studies were not obtained for 42 per cent because the patients were improving clinically and were negative. Relapses were 3.9 per cent and were subsequently rehospitalized.

Revealing New Method

Hentel, Longfield and Gordon of Albuquerque presented a well-documented and beautifully-illustrated study of the anatomic aspects of bronchiectasis. Important relevant information obtained by the fume fixation-inflation method was presented. It was pointed out that it was possible by this procedure, particularly by three-dimensional histologic studies, to distinguish definitely congenital bronchiectasis from pyogenic bronchiectasis.

Idiopathic Mediastinitis

Hache, Bernatz and Woolner of the Mayo Clinic offered a clear-cut presentation of idiopathic fibrous mediastinitis. Problems of pathogenesis, symptomatology and diagnosis were reviewed with competence. Detailed discussion of prognosis and management was part of the presentation. Of the 20 patients with this condition studied by the authors, 12 had either complete or partial superior vena caval obstruction, four had involvement of the tracheobronchial structures, two had esophageal obstruction and one died of stenosis of the pulmonary vein. In one, the mediastinal disease was found at necropsy. Surgical treatment is concerned mainly with superior vena caval obstruction, the effective relief of which still awaits further perfecting of grafting material and procedures. The overall prognosis is good, as the disease progresses slowly and the complication results usually from the slow contraction of scar tissue. Exception is made in stenosis of the pulmonary vein; all six patients so affected died of this complication.

Fate of Patients with Open-negative Cavity Syndrome

Raymond F. Corpe and Frank A. Blalock of the Battey State Hospital, Rome, Georgia, found that of 14,697 patients discharged from their hospital between January 1, 1953 and December 31, 1960, approximately 400 cases met criteria to be classified as open-negative. A yearly follow-up has been carried out. The bacteriologic relapse rate in this group of patients was about 4½ per cent and the total death rate is approximately 12 per cent. The bacteriologic relapse rate when compared to zero is quite good, when considering that nearly 70 per cent of these patients were colored; many of the white patients were in older age groups and nearly two-thirds of the patients were not deemed suitable surgical candidates.

Circulation of the Newborn Infant

The transitional circulation of the newborn infant has been studied by Mildred Stahlman and Robert Merrill of Nashville, and L. Stanley James, New York City, using the indicator dilution technique for the detection of the presence and direction of fetal shunts and estimation of their magnitude. Cardiogreen has been used as the indicator and a photomultiplier tube type densitometer used as a detector system. The volume of the withdrawal system was chosen so as to permit a constant withdrawal rate of 6 ml./minute without significant distortion of the dye dilution curve. They report that normal newborns have persistent shunts frequently bi-directional for the first two or three days of life, but that after this age, shunts are usually not detectable with this technique. Pure right-to-left shunts are more common in the youngest babies and pure left-to-right shunts were more common in the older babies. It is suggested that these shunts are at the ductus level and that their magnitude and direction are the result of the relative levels of the pulmonary and systemic arteriolar tone.

Treatment of Transposition of the Great Vessels

Thomas G. Baffes of Chicago discussed his own clinical experience in over 150 cases in which partial correction of the transposition defect has been accomplished by transferring the inferior vena cava from the right atrium to the left atrium, together with the clinical results achieved by this method. Also, he presented a case in which both the first and second stages of transposition of the great vessels were done at the same time in an attempt to achieve complete correction of the transposition complex.

Pre-emphysema in Children

Roy F. Goddard, Albuquerque, stated that full-blown emphysema may occur in asthma, bronchiectasis and mucoviscidosis in children, particularly in mucoviscidosis. However, pre-emphysema (or two-thirds of the full-blown picture, namely: obstruction and hyperaeration, without destruction) occurs frequently and can be diagnosed in its early stages and treated effectively to prevent destruction and hence the full-blown emphysema from occurring.

Surgical Treatment of Lung Cysts

June M. Fisher and George N. Bedell of Iowa City studied 22 patients with roentgenographic evidence of unilateral or bilateral air cysts. The patients were divided into two classes on the basis of clinical findings and pulmonary function tests: patients with localized cysts (Class A); and patients with diffuse emphysema and cysts (Class B). Class A patients are younger, have symptoms of shorter duration and commonly have upper lobe involvement. Cysts are more often found in the bases and are frequently multiple in Class B patients. Comparison of preoperative pulmonary function tests in the groups revealed increased residual volume and uneven distribution of inspired air in both groups, carbon dioxide retention and significant reduction in maximal breathing capacity, maximal expiratory flow rate, and vital capacity in patients with diffuse emphysema. Thirteen patients with localized cysts had surgical treatment. Postoperative pulmonary function studies showed slight increase in vital capacity and maximal breathing capacity, minimal decrease in residual volume, improved distribution of inspired air, and return to normal arterial saturation. Patients with localized cysts can have their cysts removed with benefit, but patients with diffuse emphysema should have cysts removed only in special circumstances.

Prognosis following Pneumonectomy

James J. Rams, *et al.* of Chicago related that pneumonectomy is frequently the treatment of choice for lung lesions, but the patient is often functionally incapacitated because of cardiopulmonary complications. In recent years, as a routine step of the operative procedure at the time of pneumonectomy and prior to ligation of any hilar structures, pulmonary artery pressures have been measured before and during "trial" occlusion of the vessel. The postoperative courses of these patients have been analyzed with regard to the development of cardiopulmonary complications, *i.e.*, pulmonary insufficiency, cor pulmonale, and congestive heart failure. Correlation of data indicates the group of patients with resting abnormal pulmonary artery pressures and marked elevations on occlusion of the vessel are most susceptible to cardiopulmonary complications referable to pulmonary hypertension. The method of operative measurement of pulmonary artery pressures is simple and does not require special instruments or technicians. It is felt that operative pulmonary artery pressures before and after occlusion are helpful in judging the extent of resection, as well as the postoperative management of these patients.

Digitalis in Heart Block

Vallee L. Willman, St. Louis, and co-workers investigated the effect of digitalis on circulatory dynamics in 15 dogs with complete heart block produced by ligation of the bundle of His. Digitalis in the usual dosage of 0.03 mg./Kg. reduced cardiac rate and lowered cardiac output slightly. Stroke work remained the same or was increased. Isometric ventricular tension and myocardial oxygen consumption were unchanged. Atropine abolished the slowing, suggesting that there is a vagal effect acting distal to the A-V node. Digitalis given in amounts greater than 0.05 mg./Kg. resulted in tachycardia. The increase in rate varied from ten beats per minute up to a tachycardia of 180 per minute. This increased rate was associated with increased cardiac output up to four times the predigitalization level. Isometric ventricular tension was increased up to two times control values.

Studies of Induced Hypothyroidism in Treatment of Heart Failure

Joseph M. Merrill of Nashville and John H. K. Vogel of Denver reported their observations on the effects of hypothyroidism on hemodynamic function in a group of patients with severe heart failure. After the development of hypothyroidism, patients noted symptomatic improvement with decreased dyspnea, orthopnea and fluid retention with an increase in exercise tolerance. Hemodynamic studies revealed a decrease in heart rate, cardiac index, oxygen consumption, external ventricular work and minute ventilation. There was an increase in stroke index, A-V oxygen difference and systemic resistance. The hemodynamic changes provide a partial explanation for the symptomatic improvement noted by the patients.

The August issue of *Diseases of the Chest* will carry additional scientific reports of the 27th Annual Meeting, including panel discussions, round table luncheons, cine-symposiums.

COLLEGE FELLOWS RECEIVE AWARDS

The following Fellows of the College were honored by the Industrial Medical Association at its 46th Annual Meeting in Los Angeles, April 11-13: **Dr. Oscar A. Sander,** Milwaukee, received the Knudson award for his contribution to the understanding of occupational pulmonary diseases; **Dr. G. W. H. Schepers,** Wilmington, Delaware, received the Merit in Authorship Award for the most significant contribution to the current literature of industrial medicine during 1960. Dr. Schepers wrote a series of three articles which were published in ***Industrial Medicine and Surgery*** under the title, "Theories of the Causes of Silicosis."

Dr. Herman J. Moersch, Rochester, Minnesota, Director of Education and Research of the College, was given the Chevalier Jackson Award of the American Bronchoesophagology Association at their annual meeting in Lake Placid, New York, May 23. Dr. Moersch is the second physician to receive this award, the first being Dr. Louis H. Clerf, Fellow Emeritus of the College.

Dr. Leo G. Rigler, Los Angeles, was awarded the Gold Medal of the American College of Radiology at their annual meeting in Chicago recently.

Dr. Clarence Crafoord, Stockholm, Regent of the College for Sweden, was honored by a special award presented by the Alton Ochsner Foundation for his distinguished services in cardiovascular surgery.

ANNOUNCEMENTS

The Department of Laryngology and Bronchoesophagology of Temple University Medical Center, will present a Postgraduate Course in bronchoesophagology September 11-22, 1961 and January 15-26, 1962, under the direction of Drs. Charles M. Norris and Walter H. Maloney. An application and further information may be obtained by writing to: Chevalier Jackson Clinic, Temple University Medical Center, 3401 North Broad Street, Philadelphia 40.

The University of Illinois College of Medicine, Department of Otolaryngology, will offer an intensive postgraduate basic and clinical program under the direction of Dr. Emanuel M. Skolnik. Designed for practicing otolaryngologists, it offers a compact program of one week of daytime and evening sessions to bring specialists a wide variety of current advances in management, therapy and philosophies. A review of basic morphologic features under the direction of Drs. Maurice F. Snitman and Frederic J. Pollock will also be included and will feature laboratory demonstrations, dissection and prosection, all augmented by visual aids. Interested physicians may write directly to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12.

BOOK REVIEWS

RESUSCITATION OF THE NEWBORN INFANT. Edited by Harold Abramson, C. V. Mosby Company, St. Louis, 1960, 274 pages, 36 illustrations.

This volume is additional evidence of the value of multidisciplinary approach to problems of the newborn infant. It represents collaborative efforts of distinguished individuals from the disciplines of pediatrics, anesthesiology, internal medicine, physiology, pharmacology, obstetrics, preventive medicine and public health, statistics and pathology. It is a well-integrated, sequential presentation without unnecessary repetition. Information is authoritative, complete, up-to-date and covers all important modern viewpoints. Text is supported by excellent tables and illustrations, valuable bibliographies at the end of each chapter and a pertinent glossary.

The role of the anesthesiologist in clinical management of the asphyxiated newborn is emphasized. Another stimulating idea is that of a recovery nursery for newborn infants. Benefits of such a unit are described, as well as practical pertinent details. Of considerable interest to chest physicians are chapters discussing conflicting opinions about structure and function of the fetal lung, mechanics of initial lung expansion, use of the ECG and electronic monitoring of the fetus, section on various types of mechanical resuscitators and on special laboratory procedures.

There are a few questionable opinions, such as the statement that "The Coombs' test should be made on specimens of all cord blood at the time of delivery, regardless of the Rh status of the mother." Also, remarks on hypnosis fail to indicate controversial nature of this method. Despite these, and a number of flaws in printing, this excellent volume achieves its objectives of discussing what is known and what is not known, and of suggesting stimulating paths of new investigations. It is recommended to all concerned with this problem from house staff to postgraduates.

ROBERT S. MENDELSOHN, M.D.

TREATMENT OF CANCER AND ALLIED DISEASES (VOLUME 4, TUMORS OF THE BREAST, CHEST AND ESOPHAGUS), (second edition). Edited by George T. Pack and Irving M. Ariel, Paul B. Hoeber, Inc., New York, 1960, 667 Pages, $30.00

This volume should be of value to all clinicians interested in diseases of the chest. An excellent description of all currently accepted methods of treatment for all neoplasms which arise in or extend into the thoracic cage and its contents is presented. The thorax is treated as an anatomic unit, which pertains to the specialty of thoracic surgery, **plus** breast carcinoma. Sixty-seven authors have combined their vast clinical experience to make this a comprehensive volume on surgical technique as well as a detailed textbook on radiation therapy covering the use of the most widely available energy sources, such as cobalt-60 and radioisotopes.

The editors have included all currently accepted techniques, with their limitations and accomplishments, so that the reader will have at hand the information required for deciding on the best course of treatment available today for a particular cancer patient.

MINAS JOANNIDES, JR., M.D.

SURGERY OF THE ESOPHAGUS. R. W. Postlewait and W. C. Sealy, Charles C Thomas, Springfield, 1961, 482 pages, $30.00

A well planned, masterfully organized and executed authoritative treatise which is destined to become and remain a classic for years to come. All disorders of the esophagus as they confront the physician, and particularly the thoracic surgeon, are clearly discussed and the surgical treatment detailed. To the authors' experience and results are added those of numerous other authorities in this field. The comparative statistics which are presented are extremely valuable. There is good discussion of the embryology, anatomy, and physiology of the esophagus. The illustrations are pertinent, of good quality, and the workmanship of the entire book is excellent and in keeping with this publisher's reputation. There is an extensive bibliography. This much needed volume is a must for the library of every surgeon, particularly the thoracic surgeon in training, as well as those in practice, teaching and in research.

KARL P. KLASSEN, M.D.

CLINICAL APPLICATIONS OF BRONCHOLOGY. Dezso Kassay, McGraw-Hill Book Company, Inc., New York, 1960, 225 pages

This book is an excellent, concise review of bronchial anatomy, physiology, pathology from standpoint of endoscopist. Basic concepts are well illustrated by specimen photographs, diagrams, x-rays (unfortunately printed in negative), case histories. Bronchial and segmental anatomy and terminology given in detail stressing author's views, without embryology or the anomalies. Practical coverage of accepted concepts of physiology of respiration and bronchial obstruction. American and European bronchoscopic instrumentarium, techniques described and illustrated. Two-thirds of book brief with clear descriptions of endoscopic aspects of bronchopulmonary disease including infectious and allergic bronchitis, cysts, bronchial trauma, lung abscess, bronchiectasis, tuberculosis, fungus infections, tumors, foreign bodies. Format and printing excellent. Book is review of current bronchology of interest to general physician as well as internist, pediatrician, radiologist, otolaryngologist, thoracic surgeon.

PAUL H. HOLINGER, M.D.

ATRIAL ARRHYTHMIAS, DIGITALIS AND POTASSIUM by Bernard Lown, M.D., and Harold D. Levine, M.D.

Lown and Levine have defined paroxymal auricular tachycardia (P.A.T.) with block as an auricular rate of 150-250 with an isoelectric baseline between the P waves and with spontaneously induced secondary or variable A-V block. This arrhythmia has been confused with sinus arrhythmia, atrial premature beats, and nodal tachycardia. They have pioneered our understanding of this arrhythmia although part of their story was described in their previous book entitled ***Current Concepts in Digitalis Therapy***. In the present narrat[i]ve they have described 112 episodes of this arrhythmia in 88 digitalized patients stressing its frequency, electrocardiographic distinctiveness, usual precipitation by digitalis and response to potassium treatment. The clinical importance of this arrhythmia, which discloses usually no ausculatory findings, is that it aggravates congestive heart failure and accelerates either the ventricular rate of the development of digitalis toxicity or both. They have stressed that "patients may become completely undigitalized or toxic while maintaining constant digitalis intake."

The serious prognosis of P.A.T. with block is indicated by the fact that 58 per cent of their patients died when the arrhythmia was caused by digitalis and 75 per cent died when potassium predisposed to it. They believe that these high figures are due to lack of recognition of this arrhythmia and its identification as a form of digitalis intoxication.

The authors have paid scrupulous attention to proof of causal relationship between P.A.T. with block and digitalis and potassium. This is a wise and imaginative book pillared on carefully planned clinical and animal experiments and it will stoke the thinking of the clinician, the physiologist, and the pharmacologist.

STEPHEN R. ELEK, M.D.

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CALENDAR OF EVENTS

National and International Meetings

Interim Session, American College of Chest Physicians
Denver, Colorado, November 25-26, 1961

7th International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
New Delhi, India, February 20-24, 1963

Postgraduate Courses

Cardiopulmonary Problems in Children
Denver, July 24-28

Occupational Diseases of the Chest
Philadelphia, September 25-29

Clinical Cardiopulmonary Physiology
Chicago, October 23-27

Recent Advances in the Diagnosis and Treatment of Heart and Lung Diseases
New York City, November 13-17

Recent Advances in the Diagnosis and Treatment of Heart and Lung Diseases
Los Angeles, December 4-8

Chapter Meetings

Kentucky Chapter, Louisville, September 19
Colorado Chapter, Denver, September 30
Pacific Northwest Chapter, Portland, October 27-28
Southern Chapter, Dallas, November 4-5